September 2011 1025 VOLUME 10 • ISSUE 9

ORIGINAL ARTICLE

Journal of Drugs in Dermatology

A Comparative Study of the Safety and Efficacy of 75% Mulberry (*Morus alba*) Extract Oil Versus Placebo as a Topical Treatment for Melasma: A Randomized, Single-Blind, Placebo-Controlled Trial

Glen Alvin MD, Nino Catambay MD, Ailynne Vergara MD, Maria Jasmin Jamora MD

Skin &Cancer Foundation (SCF), Manila, Philippines

ABSTRACT

Background: Melasma is an aesthetically undesirable skin condition which remains difficult to treat. Mulberry is a whitening agent with antioxidant properties.
Objective: To evaluate the safety and efficacy of 75% mulberry extract oil as a treatment for melasma versus placebo.
Patients and Methods: 50 patients were recruited and randomly assigned into two groups, with 25 treated with 75% mulberry extract oil and the other 25 treated with placebo. All patients had a negative repeat open application test (ROAT) to both mulberry extract and placebo. Patients were followed up regularly at four-week intervals for a total of eight weeks. The severity of the melasma was assessed using the melasma area and severity score (MASI), Mexameter reading, melasma quality of life score (MelasQOL) and any adverse events noted.
Results: The mean MASI score significantly improved from 4.076 (±0.24) at baseline to 2.884 (±0.25) at week 8 for the 75% mulberry extract oil group while the placebo group showed an improvement of a lesser magnitude. Mexameter readings for the mulberry group showed a significant drop from 355.56 (±59.51) at baseline to 312.52 (±57.03) at week 8 compared to the placebo group, whose Mexameter readings deteriorated from 368.24 (±46.62) at baseline to 372.12 (±44.47) at week 8. The MelasQOL score also improved tremendously for the 75% mulberry extract oil group, falling from 58.84 (SD: ±3.18) at baseline to 44.16 (SD: ±4.29) at week 8, unlike the placebo group that showed a less dramatic improvement from 57.44 (SD: ±4.66) at baseline to 54.28 (SD: ±4.79) at week 8. With regards to the adverse events, only mild itching was reported in four patients from the 75% mulberry extract oil group while there were 12 cases of either itching or erythema reported from the placebo group.

J Drugs Dermatol. 2011;10(9):1025-1031.

INTRODUCTION

Melasma is an aesthetically undesirable hyperpigmentation that occurs mainly on the face, but can occur on any sun-exposed area.[1] Melasma is mainly found in women of reproductive age.[4] People with skin phototypes III-V from regions of the world with intense sun exposure are prone to developing melasma.[2,3]

Melasma can be difficult to treat, with most treatments beneficial only in the short-term and carrying associated adverse effects like irritation, contact dermatitis and leukoderma.[6] The current gold standard for treatment is hydroquinone.[7] However, there have been reports of contact dermatitis, nail bleaching and ochronosis.[8] Newer topical treatment options for melasma include lincomycin, vitamin C, soy, arbutin, linoleic acid, burner root extract, dithiaoctanediol, beta-carotene, scutellaria extract and mulberry extract.[6,9] Mulberry extract has been found to contain flavinoids and anti-oxidant properties.[10] Its tyrosinase-inhibiting activity is comparable to hydroquinone and kojic acid.[9]

The purpose of this study is to clinically evaluate the safety and efficacy of mulberry extract oil as a skin lightening agent in the treatment of facial melasma. We sought to assess the clinical response objectively by evaluating the melasma area and severity index (MASI), Mexameter readings, assessment by both the physician and a patient quality of life assessment (MELASQOL) taken at baseline and during follow ups, and noting any adverse events.

We sought to assess the clinical response objectively by evaluating the melasma area and severity index (MASI), Mexameter readings, assessment by both the physician and a patient quality of life assessment (MELASQOL) taken at baseline and during follow ups, and noting any adverse events.

MATERIALS AND METHODS

The study was a randomized, single-blind, placebo-controlled, full-face, open 2-arm trial over a period of eight weeks, conducted on melasma subjects who voluntarily joined the study at the dermatology outpatient department at a charity hospital in Manila.

The protocol was submitted to the institutional Ethics Review Board and received its approval. An orientation of the research team consisting of the principal researcher and two clinical investigators to the protocol was done before starting the study. The clinical investigators were responsible for screening the possible subjects and explaining the objectives of the study procedures, duration and the potential benefits and risks of participation. Written instruction and informed consent were obtained from each of the patients" to "Informed consent was obtained from patients and written instructions given. Each participant was assured by the investigator that all information and results obtained from the study would remain strictly confidential. Subjects were free to withdraw their participation from the study at any time. Any adverse effects from use of the treatment creams would be appropriately treated and medication would be given free of charge.

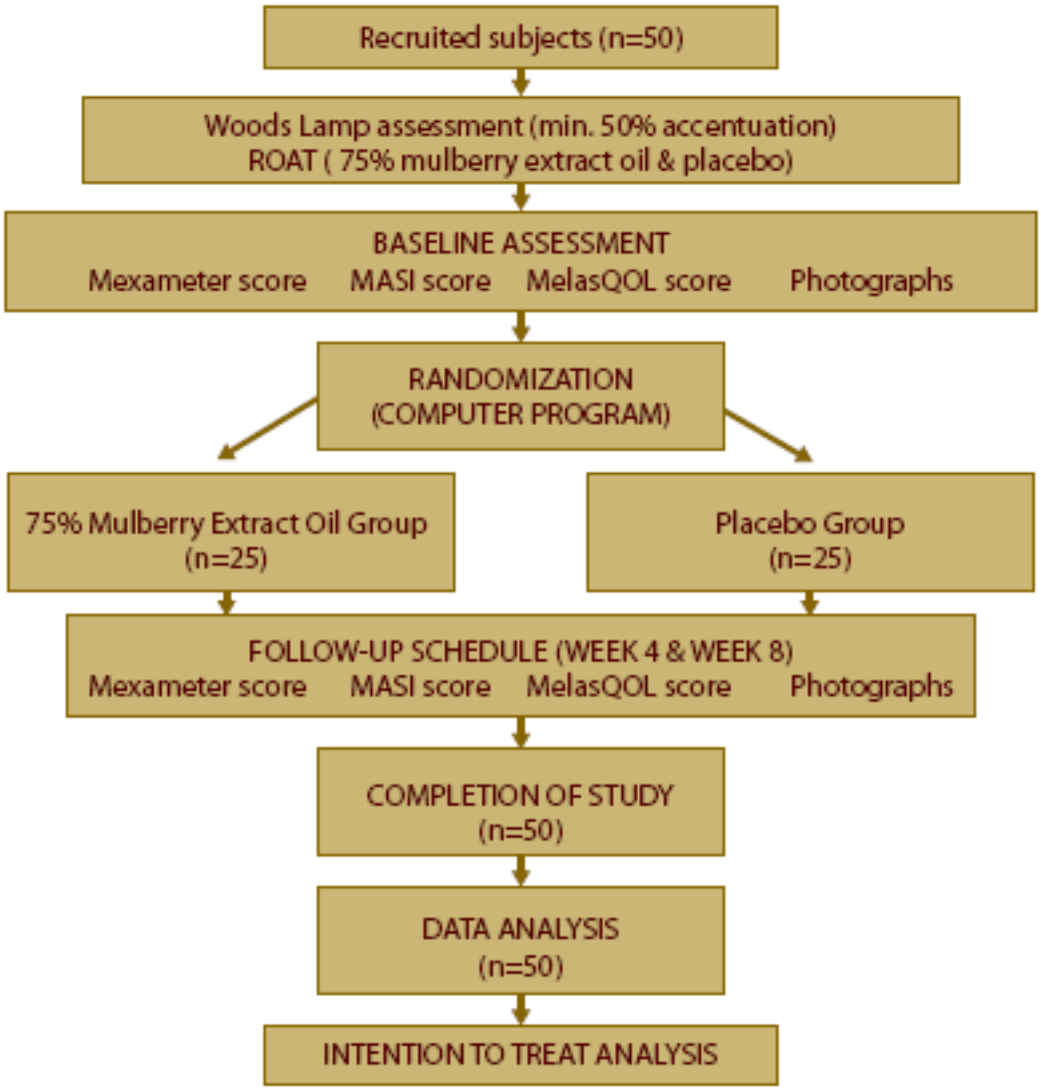
Subjects were healthy adults of ages ranging between 18 to 60 years old, with modified Fitzpatrick skin phototpes III-V, had melasma with an accentuation of at least 50 percent on Wood's light examination and were not hypersensitive to either mulberry extract or placebo. Exclusion criteria included: pregnant or nursing mothers; other pigmentary disorders; tretinoin, hydroquinone or other bleaching cream or oral contraceptive use in the past six months. All subjects enrolled had a negative repeat open allergy test (ROAT) to 75% mulberry extract oil and placebo.

Fifty (50) adult patients (49 females, one male) were included in the study. A computerized randomization plan was used to randomly assign the patients to two groups: group A (75% mulberry oil extract) and group B (placebo). Subjects were randomly assigned to apply either mulberry extract (75% mulberry in a coconut oil base) or placebo (virgin coconut as base). The samples were placed in identical pre-packed labeled bottles. The degree of hyperpigmentation was determined using a Mexameter. Reading was taken from the face (cheeks, forehead and chin). The digital Mexameter (Mexameter MX18, CK Electronic, Germany) provides an objective reproducible measurement of the two components of skin color, erythema (hemoglobin) and melanin. The MASI score was created by Kimbrough-Green to assess the area and severity of melasma. [17] Standard photographs of the subjects were taken from the front, right and left aspects of the face to highlight the hyperpigmented lesions. The subjects were also interviewed by the clinical investigator regarding their quality of life since developing melasma, based on the survey questions on the MelasQOL Score questionnaire. All subjects were instructed to apply the topical oil twice-daily to the hyperpigmented lesions on the face. They were also given sunblock with SPF 30 which was to be applied to their whole face every morning 30 minutes after applying their designated topical treatment. Subjects were advised to use an unscented soap to wash the face and to avoid unnecessary sun exposure throughout the duration of the study. Subjects were followed up regularly at four-week intervals for a total of eight weeks.

The mean change in MASI scores and Mexameter reading were calculated using the Mann-Whitney test,

while clinical scores between the treatment groups during follow ups were statistically analyzed using the repeat manner ANOVA test. The percentage of patients without adverse reaction was statistically calculated using the test of two proportions. Figure 1 shows a flow chart of the methodology and data analysis for the study.

FIGURE 1. Flow chart of the methodology and data analysis.



RESULTS

Demographic Data

The subject population consisted of 49 females (98.0%) and one male (2%) with ages ranging from a minimum of 25 years to a maximum of 60 years old. The mean age of the study population was 44.5±7.5 years. The subjects were divided into two groups consisting of 25 subjects. All of the 50 subjects completed the study.

The mean age of subjects in group A was 46.6±8.4 years. The mean age of subjects in group A was significantly older than the mean age of subjects in group B 42.4±6.0 (P value=0.031). Further statistical analysis using the Mann-Whitney test proved that the comparison of the age distribution of subjects between the two treatment groups was not statistically significant (P value=0.072). Figure 2 shows the age distribution

of subjects in the two groups.

With regards to the characteristics of melasma, the majority of the subjects in both treatment groups had a centrofacial pattern, bilateral involvement, mixed type melasma with a 1-5 year duration. Likewise, for both treatment groups, most of the subjects had no history of sun block use. Table 1 shows the detailed baseline characteristics of the subjects.

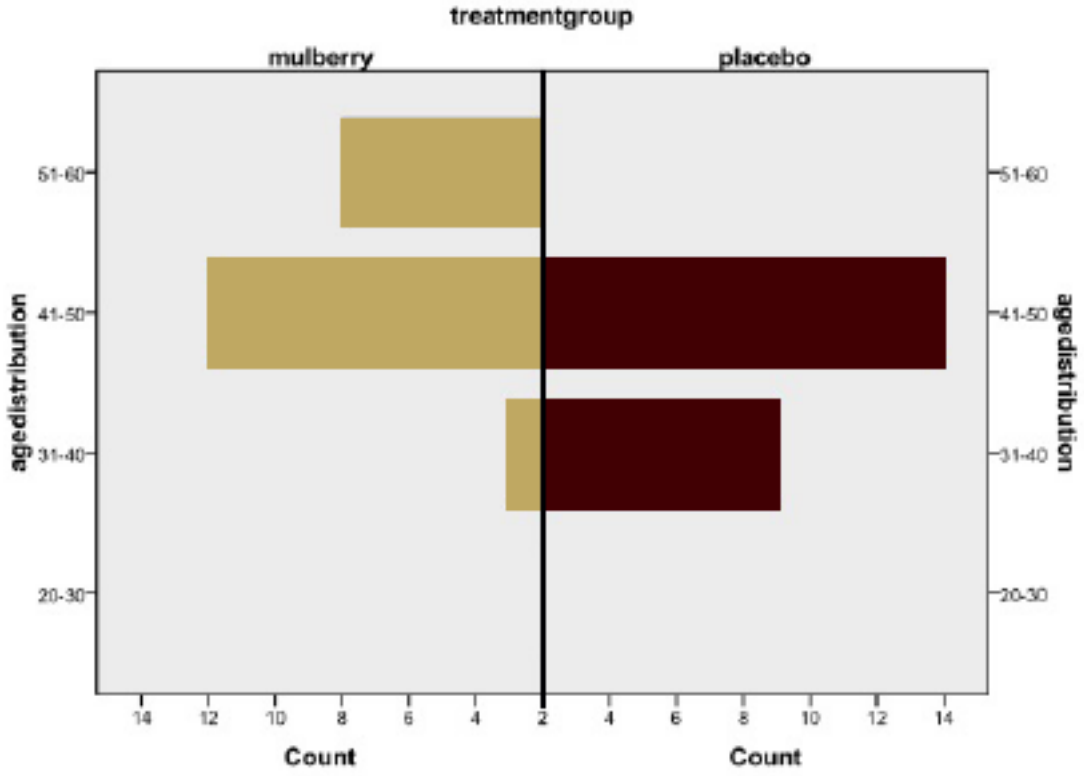
Results

Table 2 shows a comparison of the efficacy of 75% mulberry extract oil versus placebo as a topical treatment for melasma using the MASI scores, Mexameter reading and MelasQOL score as clinical parameters.

MASI Score

The findings for MASI score using the Mann-Whitney test showed that the 75% mulberry extract oil had a slightly higher baseline value (mean: 4.076, SD: ±0.24) compared to the placebo group (mean: 3.484, SD: ±0.52) and this was statistically significant (P<0.05). The computed mean MASI score for the treatment groups starting

FIGURE 2. Age distribution of subjects randomized to 75% mulberry extract oil versus placebo.



from baseline to week 8 using the Repeated Measures ANOVA test within subjects showed progressive improvement for the 75% mulberry extract oil group (P‹0.05). The mean difference in MASI score from baseline to week 8 for the 75% mulberry extract oil group was 1.19 while the placebo group had a mean difference of only 0.06 for the same period. Overall, there was a significant improvement in the MASI score from baseline to week 8 for the 75% mulberry extract oil group. Figure 3 shows a linear graph of the MASI scores from baseline to week 8 for the two groups.

Mexameter Reading

Mexameter reading at baseline exhibited a slightly lower value for the 75% mulberry extract oil group (mean: 355.56, SD: ±59.51) compared to the placebo (mean: 368.24, SD: ±46.62) but this difference was not statistically significant (P>0.05). The computed mean Mexameter reading for the treatment groups starting from baseline to week 8 demonstrated a difference for the 75% mulberry extract oil group that was significant (P‹0.05) with decreased Mexameter values indicating a lightening of the pigmentation. The placebo group

actually showed a slight increase in Mexameter reading values. Figure 4 shows a linear graph of the Mexameter reading from baseline to week 8 for the two groups.

Quality of Life Assessment

Analysis of the MelasQOL data from the two treatment groups using the Mann-Whitney test showed that at baseline, the 75% mulberry extract oil group had a MelasQOL score of 58.84 (SD: ±3.18) while the mean baseline MelasQOL score for the placebo group was 57.44 (SD: ±4.66); this difference between the two groups was found to be not statistically significant ($P<0.05$). At week 8, the MelasQol score for the 75% mulberry extract oil group improved to 44.16 (SD: ±4.29) while the placebo group's MelasQOL score was 54.28 (SD: ±4.79); this difference in the MelasQOL score between the two groups was now significant ($P<0.05$). The MelasQOL score pre- and post-treatment for the two treatment groups showed a general improvement using the Repeated Measures ANOVA test. Figure 5 shows a bar chart of the MelasQOL scores from baseline to week 8 for the two groups.

Adverse Events

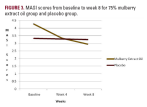
There were 16 reported cases of adverse events, four from subjects in the 75% mulberry extract oil group and 12 from the placebo group subjects. The complaints included erythema and itching. At week 4, four cases in the 75% mulberry extract oil group experienced a mild itching. In the control group, two cases reported a mild pruritus and erythema at week 4, while another two experienced a mild pruritus only. At week 8, there were four reported cases of adverse effects, all from the subjects in the control group. All four subjects had a mild pruritus, with two reporting having mild erythema as well. None of the subjects developed any serious adverse reactions that required treatment or dropping out of the study. All the subjects that reported adverse

TABLE 1.

Patient Demographics

Subject Characteristic	Treatment Group		Total n=50	*P* value
	Mulberry group n=25	Placebo group n=25		
Subject Characteristic	Treatment Group	Total	0 (0%)	0 (0%)
Age distribution, (%)				0.072
• 20–30 years	2 (8.0)	0	2	
• 31–40 years	3 (12.0)	9 (36.0)	12	
• 41–50 years	12 (48.0)	14 (56.0)	26	
• 51–60 years	8 (32.0)	2 (8.0)	10	
Gender distribution, (%)				
• Female	25 (100.0)	24 (96.0)	49	1.00
• Male	0	1 (4.0)	1	
Type of melasma, (%)				
• Epidermal	2 (8.0)	1 (4.0)	3	0.500
• Mixed Type	23 (92.0)	24 (96.0)	47	
• Dermal	0	0	0	
Melasma pattern, (%)				
• Malar	6 (24.0)	4 (16.0)	10	0.363
• Centrofacial	19 (76.0)	21 (84.0)	40	
• Mandibular	0	0	0	
Symmetry, (%)				
• Bilateral	25 (100.0)	25 (100.0)	50	*
• Unilateral	0	0	0	
Duration of melasma, (%)				
• <1 Year	3 (12.0)	4 (16.0)	7	0.500
• 1–5 Years	22 (88.0)	21 (84.0)	43	
• >5 Years	0	0	0	
History of sun block use, (%)				
• None	18 (72.0)	21 (84.0)	39	0.248
• With sun block use	7 (28.0)	4 (16.0)	11	

events were able to complete the study successfully. Figure 6 shows a photograph of one of the subjects in the study prior to applying the mulberry extract oil on her melasma and the same subject at the end of the study.



DISCUSSION

Melasma is an acquired hyperpigmentation that occurs on sun-exposed skin, presenting as symmetrical, irregular, slowly-enlarging tan-brown macules and patches. Although the precise etiology of melasma remains unknown, it is said to be multifactorial. [2] Genetic predisposition and sun exposure are major factors in the development of melasma.[2] Other factors include hormones, pregnancy, oral contraceptives and photosensitizing medications, and certain cosmetics.[2,4,5] The majority of melasma cases occur in women, most commonly during their reproductive years.[4] People with brown skin types (Fitzpatrick skin types IV to VI) from regions of the world with intense sun exposure are more prone to developing melasma.[2,3]

The most common pattern of melasma is centrofacial, which involves the cheeks, forehead, nose and chin, but it may also present in a malar or mandibular distribution.[2] Examination using Wood's lamp will identify the depth of the melanin pigmentation, thus helping to determine the type of melasma, which is classified into one of three histological types: epidermal, dermal and mixed.[2]

FIGURE 4. Mean Mexameter reading from baseline to week 8 for 75% mulberry extract oil group and placebo group.

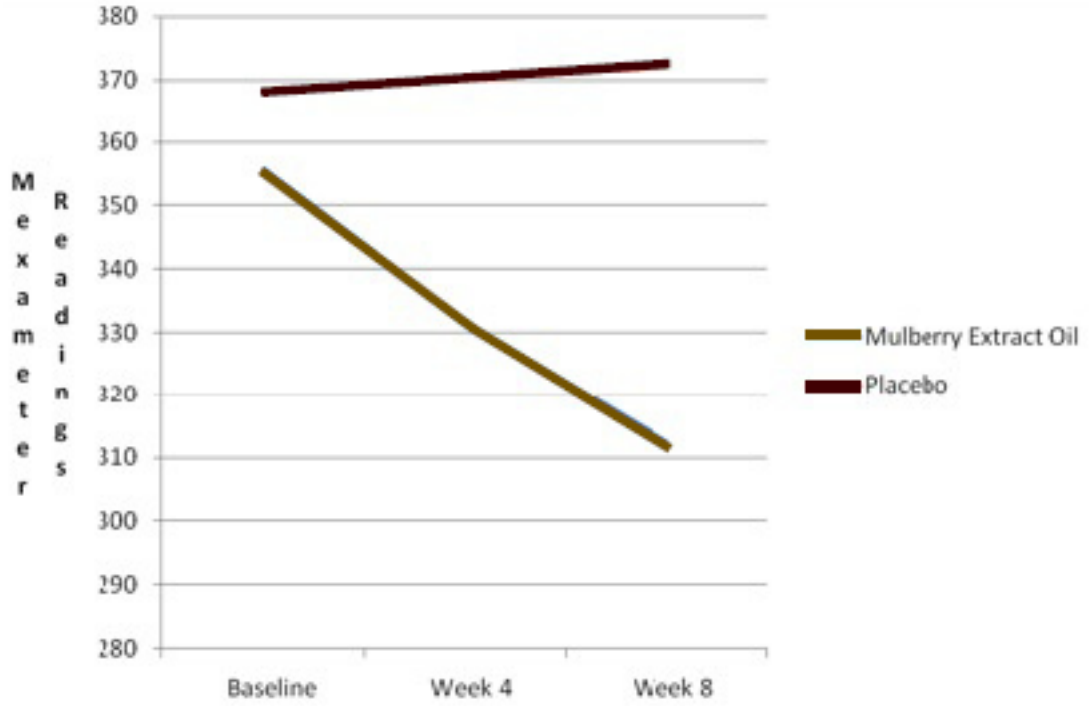


FIGURE 5. MelasQOL scores from baseline to week 8 for 75% mulberry extract oil group and placebo group.

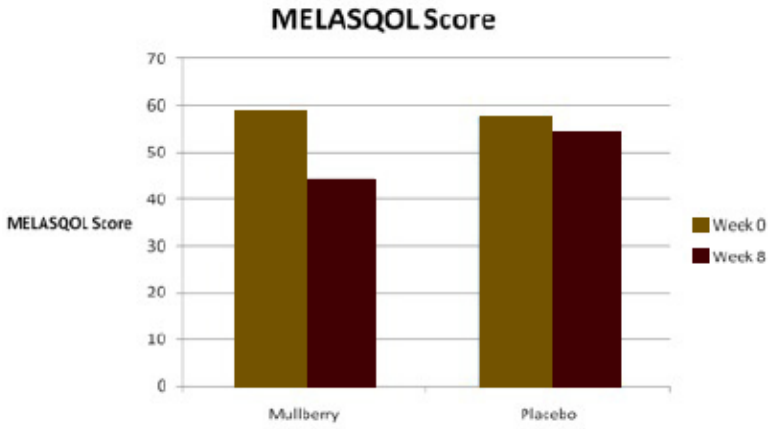
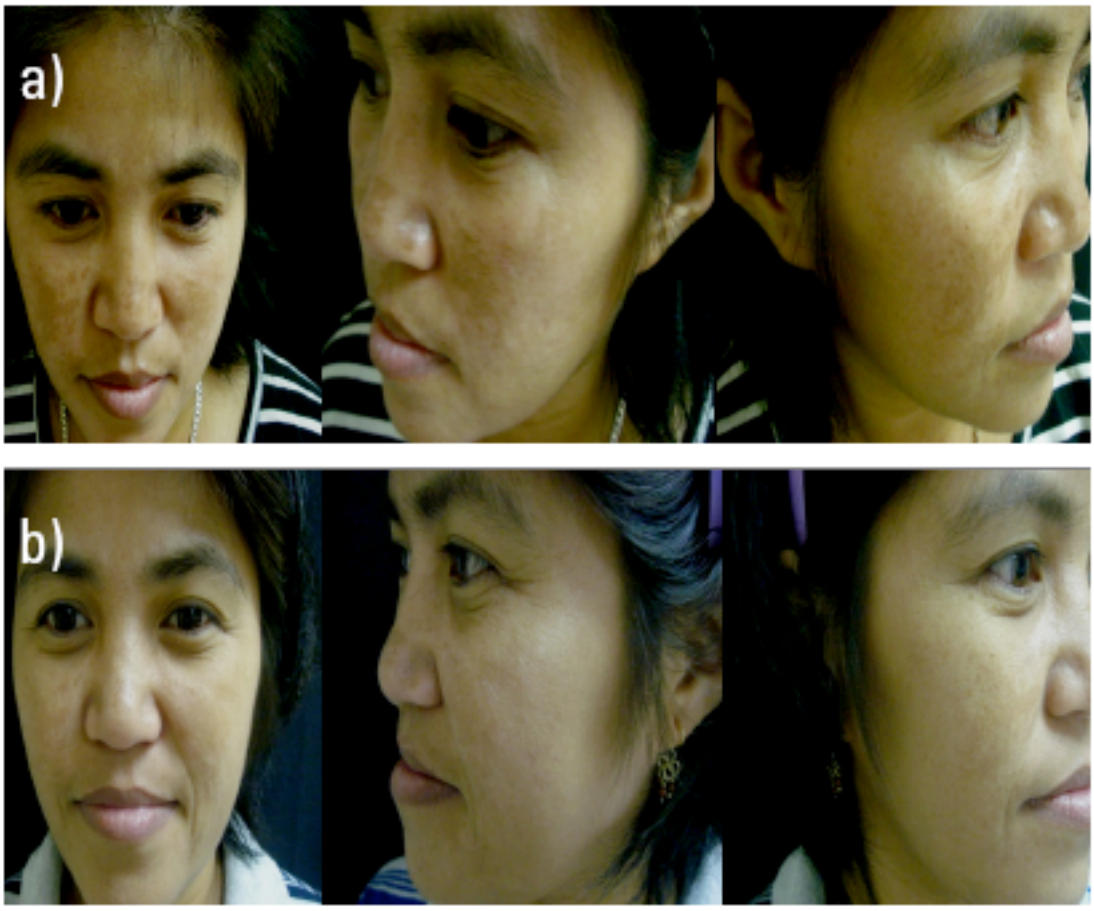


FIGURE 6. Patient in the 75% mulberry extract group **a)** before and **b)** after treatment with 75% mulberry extract oil over eight weeks. Clinical improvement was seen as improved MASI scores, Mexameter readings and MELASQOL at the end of the study period.



Demographics of our sample population were found to be similar to other reported literature on melasma in tropical regions. The majority of our subjects were from the age group of 41-50 years old. Their melasma was mainly of the mixed type with a bilateral centrofacial pattern of distribution. The lesions were found to have a duration of 1-5 years. Cestari et al. found Brazilian women with melasma to have an average age of 42 years old and mainly skin phototypes III-V as well.[11] Goh et al. found Singaporean melasma subjects to have an average age of 42 years. The subjects were of skin phototypes III-IV and had melasma for an average duration of five years. The majority of patients had a malar pattern of melasma of an epidermal type on Wood's lamp examination.[12]

Melasma is often progressive and recalcitrant to treatment with hypopigmenting agents. Anecdotal studies with modalities such as cryotherapy, medium-depth chemical peels and lasers have shown them to be effective but they may have unpredictable results and potential adverse effects that include local irritation, contact dermatitis, leukoderma and worsening hyperpigmentation. [6] The principles of melasma therapy include protection from UV light, inhibition of melanocyte activity and melanin synthesis, and the disruption and removal of melanin granules.[2] The gold standard in melasma treatment is topical hydroquinone.[7] However, reports of adverse reactions caused by hydroquinone include irritant dermatitis, hyperpigmentation, ochronosis and nail bleaching.[8]

Amongst the new generation of therapeutic armamentarium to overcome melasma are lincomycin, vitamin C, soy, arbutin, linoleic acid, burner root extract, dithiaoctanediol, beta-carotene, scutellaria extract and mulberry extract.[6,9] Most of these are already being used as an adjuvant in skin whitening products, but by themselves, they are yet to be proven effective.[9]

Mulberry extract is a natural potent antioxidant from the Morus alba plant. Zhu et al. reported that mulberry is

rich in flavinoids, which act as a tyrosinase activity inhibitor.[10] Ebanks et al. showed that the flavinoids found in mulberry have a structure similar to the dihydroxyphenyl group of DOPA, thus enabling it to inhibit the activity of the tyrosinase enzyme at the distal portion of the melanogenesis pathway.[14] It was also suggested that flavinoids have the capability to chelate copper at the tyrosinase's active site.[14] Mulberry also contains mulberroside F, which has an inhibitory effect on tyrosinase activity and also on melanin formation on melan-a cells.[10] Studies by Lee comparing the tyrosinase inhibition of mulberry revealed that 0.39&#37concentration of mulberry extract inhibits tyrosinase by 50 percent compared to 5.5 percent for hydroquinone and 10.0 percent for kojic acid.[10] Studies comparing the effects of mulberry extract against kojic acid on the inhibition of tyrosinase activity have found mulberry extract to be 4.5 times more potent as a tyrosinase inhibitor.[13] It was

TABLE 2.

Comparison of the Efficacy of 75% Mulberry Extract Oil Versus Placebo as a Topical Treatment for Melasma Among Using the MASI Score, Mexameter Reading and MelasQOL Score

Subject Characteristic	Treatment Group		*P* value
	Mulberry group n=25	Placebo group n=25	
Masi Scores			
• Baseline	4.076 (± 0.24)	3.484 (± 0.52)	0.000
• Week 4	3.296 (± 0.42)	3.456 (± 0.53)	0.496
• Week 8	2.884 (± 0.25)	3.392 (± 0.53)	0.000
P value**	0.000	0.000	
Mexameter Reading			
• Baseline	355.56 (± 59.51)	368.24 (± 46.62)	0.322
• Week 4	331.52 (± 56.13)	370.20 (± 44.23)	0.010
• Week 8	312.52 (± 57.03)	372.12 (± 44.47)	0.000
P value**	0.000	0.000	
Quality of Life			
• Baseline	58.84 (± 3.18)	57.44 (± 4.66)	0.310
• Week 8	44.16 (± 4.29)	54.28 (± 4.79)	0.000
P value**	0.000	0.000	

*computed using Mann-Whitney test, significant at $P<0.05$.
**computed using Repeated Measures ANOVA.

also discovered that mulberry had superoxide scavenging activity besides melanin synthesis inhibition and tyrosinase inhibition.[13] MASI and Mexameter reading scores in this study showed a significant improvement for the mulberry extract oil group compared to the placebo group, giving support to the above data regarding mulberry extract as a lightening agent. The fact that the placebo group also exhibited an improvement in the MASI score may be due to diligent sunblock use.[16]

The MelasQOL scale was developed by Balkrishnan in 2003.[11] The quality of life domains found to be most affected by melasma were social life, recreation and leisure and emotional well-being.[15] In our study, the MelasQOL score showed a significant improvement in the mulberry extract oil group compared to the placebo group The decrease in the MelasQOL score was seen to correlate with the improvement exhibited by both the Mexameter reading and MASI score. Erythema and pruritus were the most frequent adverse events from subjects of both groups during the entire period of our study, but were mild and did not lead to subject drop-outs.

CONCLUSION

Seventy-five percent (75%) mulberry extract oil improves melasma in skin phototypes III-V, using objective measurements including Mexameter reading, MASI scores and MelasQOL scores. This is first study on the efficacy and safety of 75% mulberry extract oil on melasma amongst Filipino women. Although this study sample is small, it demonstrated a significant improvement in Mexameter, MASI and MelasQOL scores and encountered very minimal adverse events. These indicate that 75% mulberry extract oil is a good lightening agent in melasma. The authors recommend a larger sample size to document efficacy of mulberry extract, and longer duration of treatment and follow-up to three or six months, as well as follow up after the cessation of treatment for one month. Initial photopatch testing to rule out photocontact dermatitis should also be performed. A comparative study with 4% hydroquinone, the gold standard for melasma, would be the next step in proving the worth of 75% mulberry extract oil as an effective alternative for melasma treatment.

DISCLOSURES

The authors have no relevant conflicts of interest to disclose

REFERENCES

1. Mateus A, Bravo B, Issa MC, Spinelli L. A clinical prospective, randomized, doubled-blind trial comparing skin whitening complex versus hydroquinone in the treatment of melasma. J Am Acad Dermatol. 2007;56(2):87.
2. Gupta AK, Gover MDA, Kewan N, Taylor S. The treatment of melasma: A review of clinical trials. J Am Acad Dermatol. 2006;55(6):1048-1065. Epub September 28, 2006.
3. Griffiths CE. Assessment of topical retinoids for the treatment of Far-East Asian skin. J Am Acad Dermatol. 1998;39(2 Pt 3):104S-107S.
4. Montemarano AD. Melasma. Emedicine. Available at: http://emedicine.medscape.com. Accessed November 6, 2008.
5. Hurley ME, Guevara IL, Gonzales RM, Pandya AG. Efficacy of glycolic acid peels in the treatment of melasma. Arch Dermatol. 2002;138:1578-1582.
6. Mu-Hyung L, Hyun-Jin K, Dong-JU H, Jong-Hyun P, Hong-Yong K. Therapeutic effect of topical application of linoleic acid and lincomycin in combination with betamethasone valerate in melasma patients. J Korean Med Sc. 2002;17:518-523.
7. Hexsel D, Arellano I, Rendon M. Ethnic considerations in the treatment of Hispanic and Latin-American patients with hyperpigmentation. Br J Dermatol. 2006;156(suppl 1):7-12.
8. Rendon M, Berneburg M, Arellano I, Picardo M. Treatment of melasma. J Am Acad Dermatol. 2006;54(5 suppl 2):272S-281S.
9. Badreshia-Bansal S, Draelos D. Insight into skin lightening cosmeceuticals for women of color. J Drugs Dermatol. 2007;6(1):32-39.
10. Zhu W, Gao J. The use of botanical extracts as topical skin-lightening agents for the improvement of skin pigmentation disorders. J Investig Dermatol Symp Proc. 2008;13(1):20-24. .
11. Cestari TF, et al. Validation of a melasma quality of life questionnaire for Brazilian Portuguese language: The MelasQoL-BP study and improvement of QoL of melasma patients after triple combination therapy. Br J Dermatol. 2006;156(suppl 1):13-20.
12. Goh CL, Dlova CN. A retrospective study on the clinical presentation and treatment outcome of melasma in a tertiary dermatological referral center in Singapore. Singapore Med J. 1999;40(7):455-458.
13. Lee SH, et al. Mulberroside F isolated from leaves of Morbus alba inhibits melanin biosynthesis. Biol Pharm Bull. 2002;25(8):1045-1048.
14. Ebanks JP, Wickett RR, Boissy RE. Mechanism regulating skin pigmentation: The rise and fall of complexion coloration. Int J Mol Sci. 2009;10(9):4066-4087.
15. Dominguez AR, Balkrishnan R, Ellzey AR, Pandya AG. Melasma in Latina patients: Cross-cultural adaptation and validation of a quality of life questionnaire in Spanish language. J Am Acad Dermatol. 2006;55(1):59-66. Epub May 2, 2006.
16. Vazquez M, Sanchez JL. The efficacy of a broad-spectrum sunscreen in the treatment of melasma. Cutis. 1983;32(1):92, 95-96.
17. Kimbrough-Green CK, Griffiths CE, Finkel LJ, Hamilton TA, et al. Topical retinoic acid (tretinoin) for melasma in black patients. A vehicle-controlled clinical trial. Arch Dermatol. 1994;130:727-733.

Address for Correspondence

Maria Jasmin Jamora
1311 Batangas Street
Corner of Finlandia Street
Makati City, Philippines
Phone: 006328943952
Fax: 006322396098
E-mail: jasmin_jamora@yahoo.com

FIGURE 1. Flow chart of the methodology and data analysis.

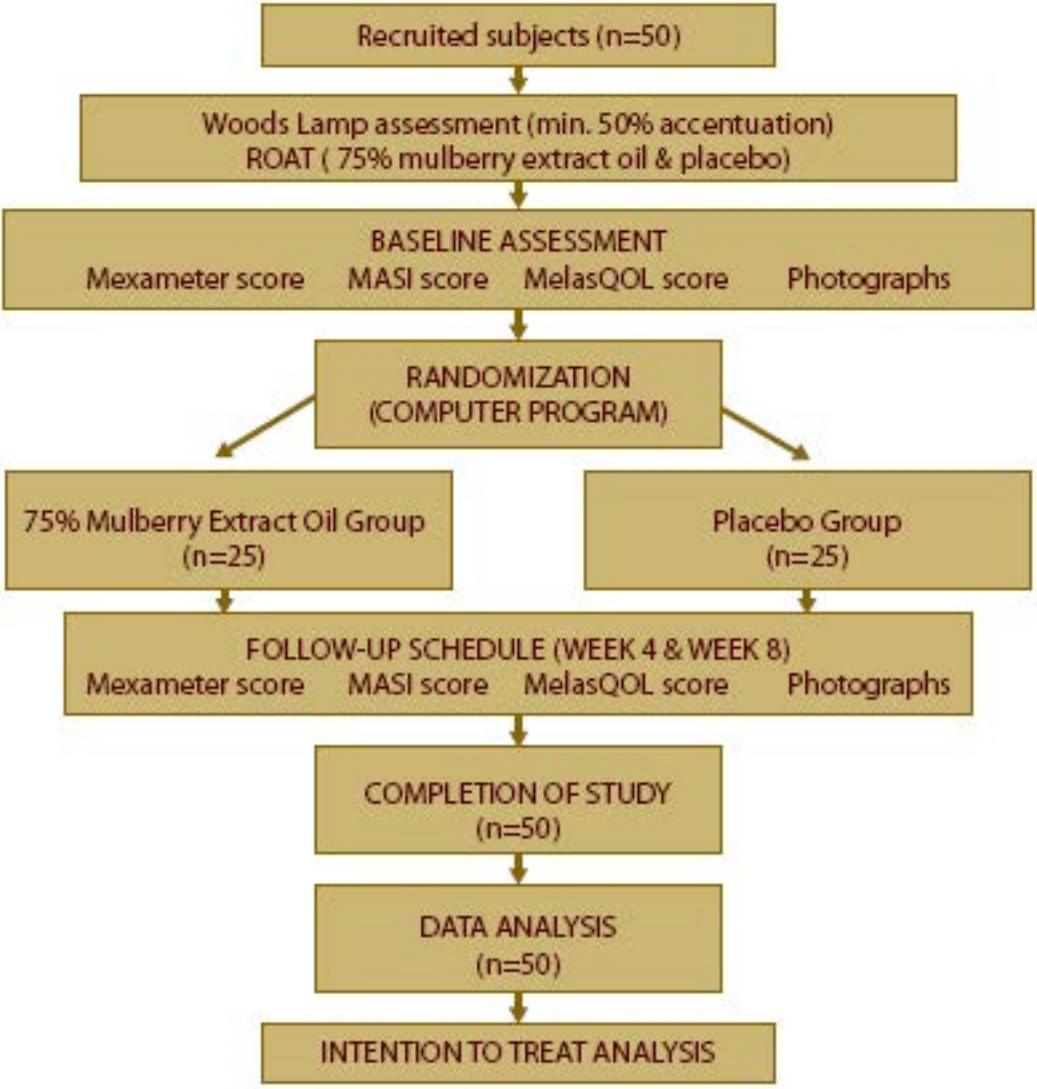


FIGURE 2. Age distribution of subjects randomized to 75% mulberry extract oil versus placebo.

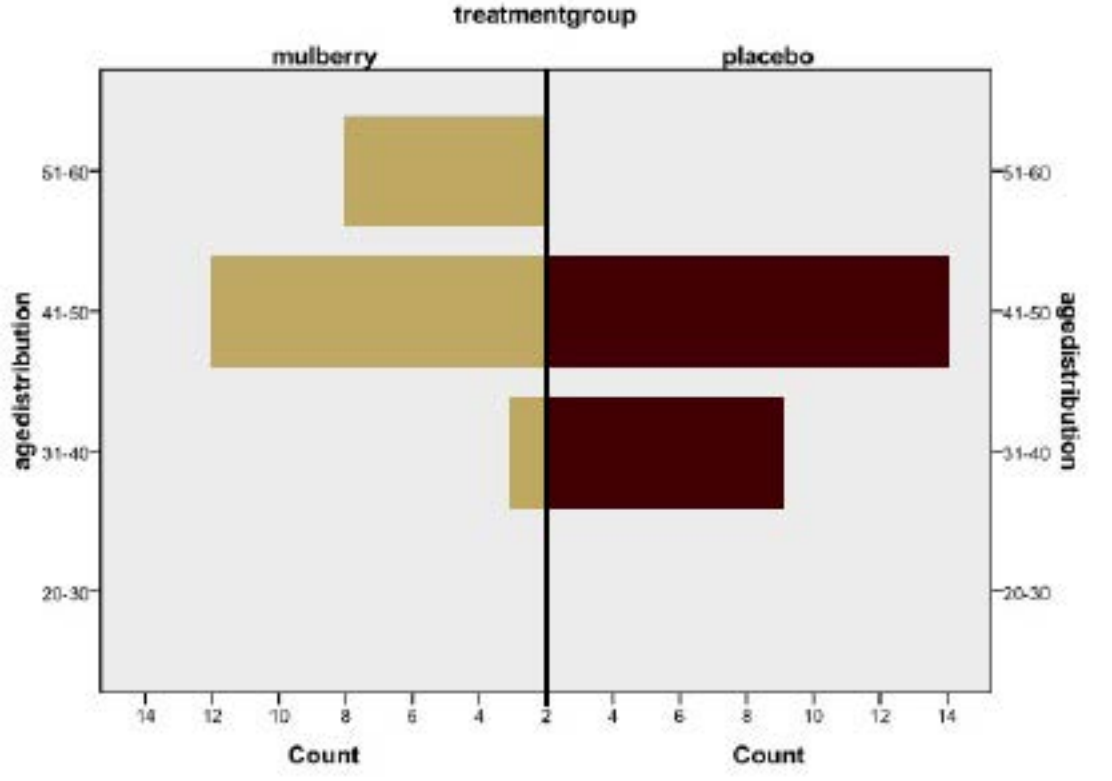


TABLE 1.

Patient Demographics

Subject Characteristic	Treatment Group		Total n=50	*P* value
	Mulberry group n=25	Placebo group n=25		
Subject Characteristic	Treatment Group	Total	0 (0%)	0 (0%)
Age distribution, (%)				0.072
• 20–30 years	2 (8.0)	0	2	
• 31–40 years	3 (12.0)	9 (36.0)	12	
• 41–50 years	12 (48.0)	14 (56.0)	26	
• 51–60 years	8 (32.0)	2 (8.0)	10	
Gender distribution, (%)				
• Female	25 (100.0)	24 (96.0)	49	1.00
• Male	0	1 (4.0)	1	
Type of melasma, (%)				
• Epidermal	2 (8.0)	1 (4.0)	3	0.500
• Mixed Type	23 (92.0)	24 (96.0)	47	
• Dermal	0	0	0	
Melasma pattern, (%)				
• Malar	6 (24.0)	4 (16.0)	10	0.363
• Centrofacial	19 (76.0)	21 (84.0)	40	
• Mandibular	0	0	0	
Symmetry, (%)				
• Bilateral	25 (100.0)	25 (100.0)	50	*
• Unilateral	0	0	0	
Duration of melasma, (%)				
• <1 Year	3 (12.0)	4 (16.0)	7	0.500
• 1–5 Years	22 (88.0)	21 (84.0)	43	
• >5 Years	0	0	0	
History of sun block use, (%)				
• None	18 (72.0)	21 (84.0)	39	0.248
• With sun block use	7 (28.0)	4 (16.0)	11	

FIGURE 3. MASI scores from baseline to week 8 for 75% mulberry extract oil group and placebo group.

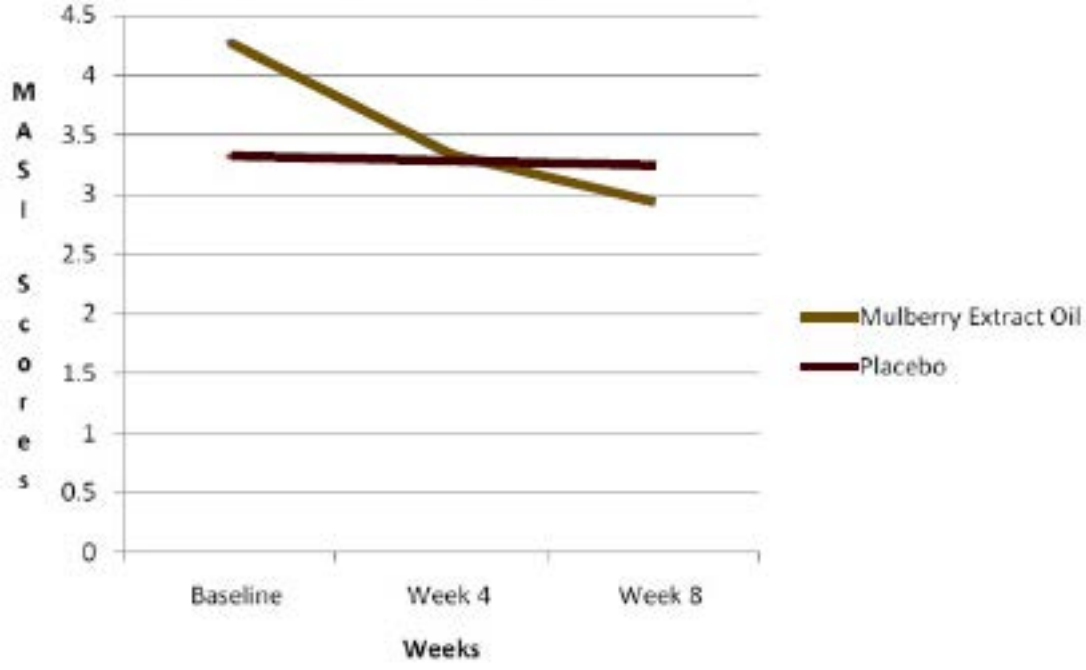


FIGURE 4. Mean Mexameter reading from baseline to week 8 for 75% mulberry extract oil group and placebo group.

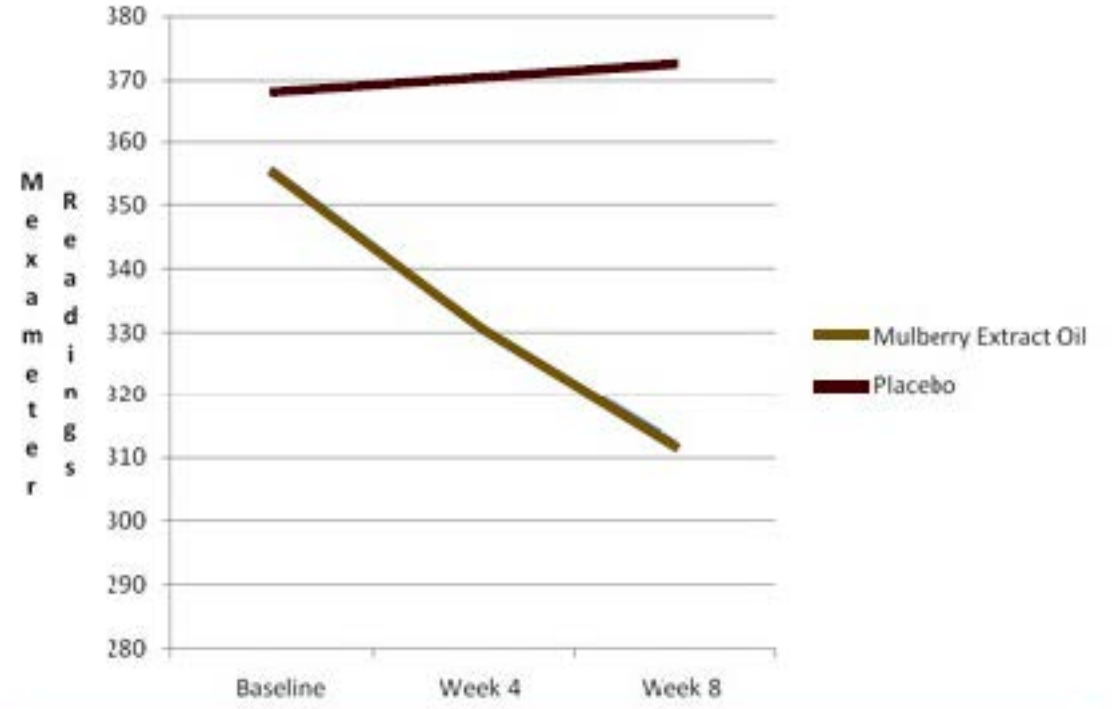


FIGURE 5. MelasQOL scores from baseline to week 8 for 75% mulberry extract oil group and placebo group.

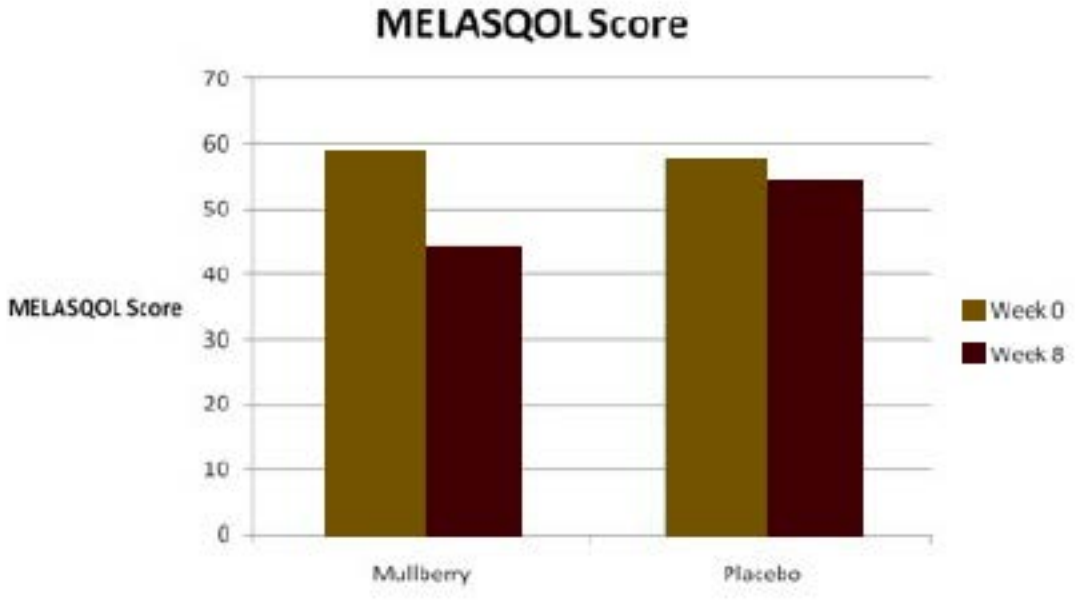


FIGURE 6. Patient in the 75% mulberry extract group **a)** before and **b)** after treatment with 75% mulberry extract oil over eight weeks. Clinical improvement was seen as improved MASI scores, Mexameter readings and MELASQOL at the end of the study period.

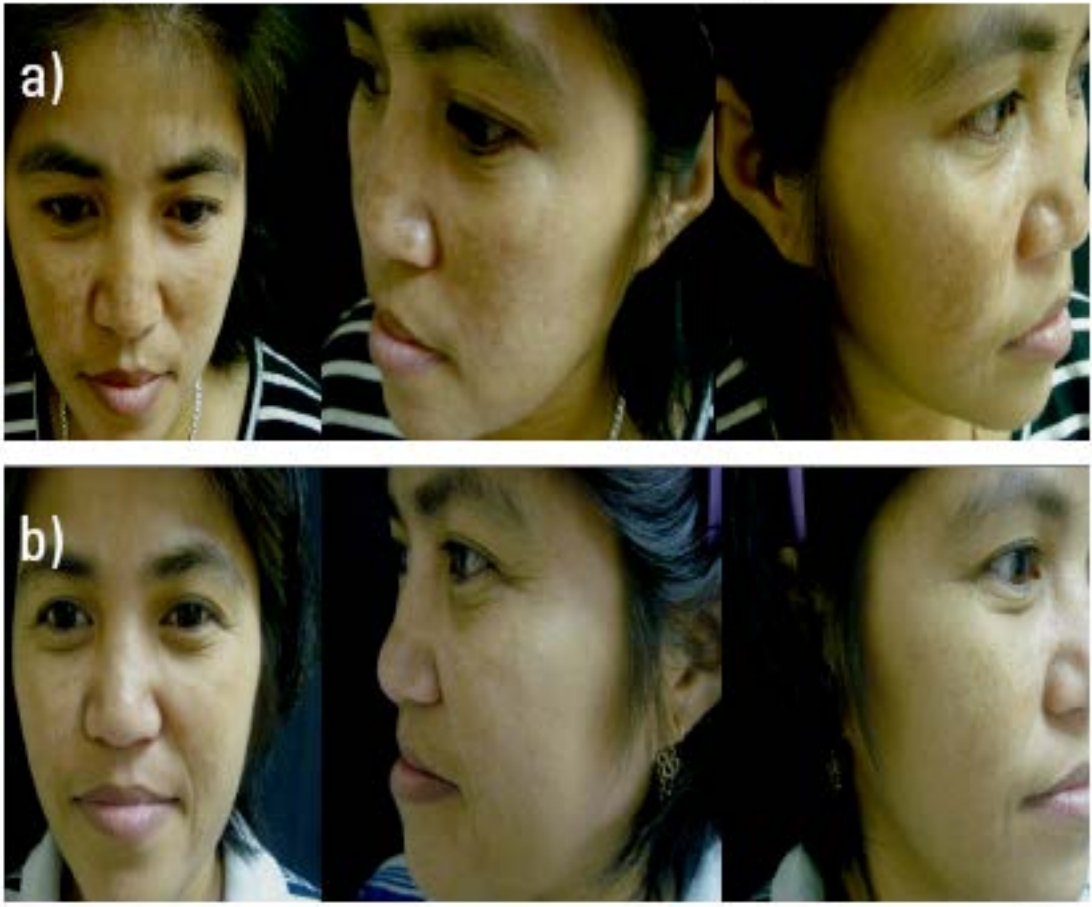


TABLE 2.

Comparison of the Efficacy of 75% Mulberry Extract Oil Versus Placebo as a Topical Treatment for Melasma Among Using the MASI Score, Mexameter Reading and MelasQOL Score

Subject Characteristic	Treatment Group		*P* value
	Mulberry group n=25	Placebo group n=25	
Masi Scores			
• Baseline	4.076 (± 0.24)	3.484 (± 0.52)	0.000
• Week 4	3.296 (± 0.42)	3.456 (± 0.53)	0.496
• Week 8	2.884 (± 0.25)	3.392 (± 0.53)	0.000
P value**	0.000	0.000	
Mexameter Reading			
• Baseline	355.56 (± 59.51)	368.24 (± 46.62)	0.322
• Week 4	331.52 (± 56.13)	370.20 (± 44.23)	0.010
• Week 8	312.52 (± 57.03)	372.12 (± 44.47)	0.000
P value**	0.000	0.000	
Quality of Life			
• Baseline	58.84 (± 3.18)	57.44 (± 4.66)	0.310
• Week 8	44.16 (± 4.29)	54.28 (± 4.79)	0.000
P value**	0.000	0.000	

*computed using Mann-Whitney test, significant at $P<0.05$.

**computed using Repeated Measures ANOVA.