

# A Pilot Study on Aloe Vera Leaf Extract in Cream Base for the Clinical Improvement of Melasma: A Split-Face Trial

## Abstract

**Introduction:** Melasma is a pigmentary disorder, generally difficult to treat, hence, the need for skin lightening agents. Recent studies found out that aloesin, a component of the aloe vera leaf extract, has a therapeutic effect on pigmentation suppression via its inhibitory effect on the tyrosinase activity. Based on these findings, aloe vera leaf extract may be used as an alternative treatment for melasma.

**Objectives:** The general objective of the study is to determine the efficacy and safety of aloe vera leaf extract in cream base for the clinical improvement of melasma among patients seen in Jose R. Reyes Memorial Medical Center, Dermatology Department, OPD

**Methods:** 35 patients (Fitzpatrick skin types III-V) diagnosed with epidermal or mixed type of melasma were given aloe vera extract in cream base to be applied over the hyperpigmented patches on the right malar area once a day. Similar cleansing soap and sunblock were given to the patients. Patient's hyperpigmented patches, both treated and untreated, were evaluated at baseline and every 4 weeks using the Mexameter. This procedure was done for a period of 12 weeks.

**Results:** Based on the target of thirty five (35) subjects, this study came up with thirty one (31) respondents due to non-follow up of 4 patients. Skin melanin index on the right malar, as measured by a mexameter, decreased continuously and this reduction in pigmentation was statistically significant at 12 weeks of treatment ( $p=0.000$ ). There was no incidence of adverse effects reported with the topical use of aloe vera extract in cream base.

**Conclusion:** Aloe Vera Leaf Extract in cream base is an effective and safe alternative treatment option for the clinical improvement of melasma.

## Introduction

Melasma is a common acquired disorder characterized by symmetric, hyperpigmented patches especially on the forehead, malar regions and upper lip [1]. Although the exact pathogenesis of melasma is unknown, it is hypothesized that following exposure to UV irradiation, hyperfunctional melanocytes within involved skin produce increase amounts of melanin. Additional important pathogenic factors include the skin phototype and estrogens and disorders such as autoimmune thyroid disease also have the potential to aggravate melasma [2]

Melasma is a very common cutaneous disorder, accounting for 0.25 to 4% of the patients seen in Dermatology Clinics in South East Asia [3]. It is most prevalent among young to middle-aged women who are Hispanic or of African, Asian or Middle Eastern descent [4]. By causing cosmetic disfigurement, melasma is an aesthetically undesirable, skin condition which is frequently associated with a significant emotional effect. Pigmentary disorders including melasma are generally difficult to treat, hence, the need for skin lightening agents including cosmeceuticals. Common topical agents currently used to treat hyperpigmentation include hydroquinone, retinoids,



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glycolic acid and azelaic acid. However, these compounds can cause adverse effects, mostly in the form of skin irritation. In addition, hydroquinone, a very effective depigmenting agent which acts via inhibiting the conversion of DOPA to melanin by inhibition of the enzyme, tyrosinase, can rarely produce an untoward skin pigmentation called exogenous ochronosis [5]. Many patients, therefore, do not tolerate such depigmenting ingredient and request milder yet efficacious compounds. Both patients and physicians are increasingly welcoming the use of depigmenting agents from natural sources in view of their high efficacy and tolerance.

In the search for novel depigmenting agents, the investigation of natural plant extracts has led to the identification of many potentially active compounds. Several studies were done to assess the medicinal properties of aloe vera and results have raised the possibility that aloesin, a chromone derivative isolated from aloe vera leaf, may be used as an agent to inhibit melanin formation induced by UV radiation by inhibiting tyrosinase activity [6-8].

We report herein a pilot study on the efficacy and safety of aloe vera leaf extract in cream base for the clinical improvement of melasma among Filipinos seen at the Department of Dermatology of the Jose R. Reyes Memorial Medical Center.

## Patients and Methods

### Study Design

This was a split-face, pilot study conducted in the Dermatology Outpatient Department of Jose R. Reyes Memorial Medical Center.

An Institutional Review Board / Institutional Ethics Committee of the Jose R. Reyes Memorial Medical Center approved the study prior to its initiation following the guidelines of good clinical practice.

### Patients

Male or female aged 18-50 years with skin type III-V, diagnosed with epidermal or mixed type of melasma clinically and classified by Wood's lamp examination were enrolled, after signing a written

**Table 1:** Demographic Characteristics.

Profile	Frequency (n = 31)	Percentage (%)	Mean±SD
Age≤ 35	5	16.1	43.2 ± 5.8
35 – 38	3	9.7	
39 – 42	5	16.1	
43 – 46≥47	11	35.5	
	7	22.6	
Gender			
Male	0	0	
Female	31	100	

informed consent form.

Pregnant women or nursing mothers using oral contraceptive pills or any cosmetic depigmenting agents (such as Hydroquinone) within 6 months prior to the study, those with known hypersensitivity to any of the components of the test medication, or with any significant medical condition or history of chronic systemic disorders were excluded. Volunteers were also excluded if they were expected to have any prolonged exposure to the sun during the study.

#### Product

The aloe vera leaf extract in cream form was prepared by the University of the Philippines-Manila, College of Pharmacy, Industrial Pharmacy Unit

#### Intervention

Patient fulfilling inclusion and exclusion criteria were instructed to wash their skin with mild cleanser and to apply the same brand of broad spectrum sunscreen with SPF 50 on the entire face every morning. The aloe vera extract in cream base was applied on the right malar area only, once a day, before bedtime for 12 weeks.

#### Clinical Assessment

Patient's hyperpigmented patches on the malar area, both treated and untreated, were evaluated at baseline and every 4 weeks using the Mexameter.

#### Safety Assessment

To evaluate the tolerability of the test cream, the subjects were asked to record any dryness, itching, stinging, redness, or scaling during the treatment period. In case of any severe adverse effects and if the participant could not continue the study, the use of cream was stopped and the measurements were done on the same or next day.

#### Statistical Analysis

Statistical analyses were performed using IBM SPSS (version 21; SPSS Inc., Chicago, IL USA) software considering 95% confidence interval in statistical data analyses. For the descriptive analysis, means with their corresponding standard deviation was used to describe the demographic characteristics of all the patients included in the study while proportion was used for the categorical data. Melanin index of the right and left malar area were presented as the mean±standard deviation. Values obtained at week 12 were compared with baseline values using paired t-test and the statistical significance was set at a p-value less than 0.05. An incidence proportion was used to determine and record the incidence of adverse effects with the topical use of aloe

vera extract in cream base.

## Results

Based on the target of thirty five (35) subjects, this study came up to thirty one (31) respondents due to non-follow up of 4 patients. The collected data on age and gender were tabulated and presented in frequency and percentage as shown in Table 1. It was revealed that all patients were female and no male voluntarily gave their consent for the study. The average age of patients was 43.2 years (SD = 5.8). The results implied that the patients' ages were significantly distributed in 31 to 51 age range interval but majority of the patients plunged in age intervals of 43 to 46 years old. The melanin index was monitored by Mexameter at baseline and after intervention at weeks 4, 8 and 12. The average level of melanin index showed a continuous reduction (Figure 1) for both the treated and the untreated areas. The reduction in melanin index for the right malar was statistically significant at week 12 (p=0.00)

(Table 2). There were no adverse effects such as erythema, pruritus, or burning noted throughout the course of treatment.

## Discussion

Melasma is a very common cutaneous disorder more frequently observed among women, accounting for 90% of cases [9]. Pigmentation disorders such as melasma, can be an issue for all individuals, especially those with skin of color [10]. Treatment of melasma is difficult and a number of agents have been used for this intractable condition. Hydroquinone, the gold standard in the treatment of hyper pigmentation for more than 50 years, is a phenolic compound that reduces the conversion of dihydroxyphenylalanine to melanin by inhibiting tyrosinase [11]. However, concerns regarding ochronosis, allergic and irritant contact dermatitis, and melanocyte toxicity



**Figure 1:** Melanin Index.

**Table 2:** The mean±standard deviation of mexameter values at baseline and at 12 weeks of treatment.

Description		Mean±SD	Significance p ≤ 0.05	Remarks
Mexameter Left Malar	Baseline	282.9±50.8	0.203	Not significant
	12 <sup>th</sup> week	281.7±49.7		
Mexameter Right Malar	Baseline	281.3±42.8	0.000	Significant
	12 <sup>th</sup> week	276.9±41.9		

have prompted a search to find alternative agents for the topical management of melasma. Aloe vera is the oldest medicinal plant ever known and has been used externally to treat various dermatological conditions due to its anti-inflammatory, anti-bacterial, anti-fungal and anti-oxidant properties [5]. Increases in the use of aloe vera leaf extract as a skin cosmetic prompted Yagi et al. to identify the active components and reported that barbaloin, 2'-o-feruloylaloenin, aloenin, and aloenin inhibit mushroom tyrosinase activity in vitro, aloenin showed higher activity than the others [7]. On the basis of these results, Choi et al. examined the inhibitory effect of aloenin on the pigmentation of human skin induced by UV radiation and found out that aloenin inhibit hyperpigmentation after UV radiation in a dose dependent manner and concluded that aloenin has a therapeutic effect on pigmentation suppression via its inhibitory effect on the tyrosinase activity [7]

In this study, it was assessed that both the right and left malar areas showed a continuous decrease in pigmentation for the treatment duration of 12 weeks. This reduction was observed as early as 4 weeks of treatment (Figure 1). The result of the t-test comparing the values taken at baseline and at 12 weeks of treatment showed a significant reduction in pigmentation for the right malar area (Table 2) and this result further suggests the effectivity of using aloe vera leaf extract in cream base for the clinical improvement of melasma.

Although the decrease in the melanin index for the left malar area was not significant (Table 2), this decrease highlights the importance of sunblock in the treatment armamentarium of melasma patients and the use of it alone, may not just control or prevent worsening of melasma but also adequate to cause a mild clinical improvement. In a study using pigmented skin equivalents (human keratinocytes and fibroblasts), aloenin induced dose-dependent reduction in tyrosinase activity and melanin content without changing the morphology of the cells, suggesting a good safety profile [11]. This pilot study further demonstrates the safety of topical application of aloe vera leaf extract in cream base which did not show incidence of adverse effects.

One limitation of this study was the lack of long-term follow-up of the subjects after the end of the trial. Also, it is recommended to assess the patient's quality-of-life as well as to do a subjective measure of improvement in addition to the objective parameter.

## Conclusion

In conclusion, the result of this pilot study suggests that Aloe Vera Leaf Extract in cream base is an effective and safe alternative treatment option for the clinical improvement of melasma. Larger randomized, controlled trials are needed to further establish its efficacy and safety.

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