

Efficacy Evaluation of Alpha-Bisabolol Whitening Cream

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Abstract

α -bisabolol extracted from German Chamomile (*Matricaria chamomilla*) was reported with anti-inflammatory effect together with a promising whitening compound. This research evaluated the whitening effect of α -bisabolol on 15 Thai women with normal skin 10 persons and hyperpigmentation skin 5 persons. The effect of whitening cream after being applied on the skin for 4 weeks was evaluated by using Mexameter to measure the melanin content and Chromameter to measure the lightness of the skin. The results in normal skin type illustrated that emulsion with α -bisabolol at concentration of 1.0 % was able to significantly decrease the maximum melanin content about 28.6 ± 15.3 ($P < 0.05$) and increase the skin lightness at significant level 3.8 ± 1.7 ($P < 0.05$). In the hyperpigmentation induced group, emulsion with α -bisabolol 0.1 % were also able to significantly decrease the melanin content at significant level 19.8 ± 3.7 ($P < 0.05$) and increase the skin lightness at significant level 4.0 ± 1.5 ($P < 0.05$) by α -bisabolol at concentration of 0.5 %. Therefore, it can be concluded that α -bisabolol is an effective as a whitening ingredient used for cosmetics. Moreover, the α -bisabolol whitening cream was proven to have a good stability and no irritation on all skin type.

Keywords: α -Bisabolol/Hyperpigmentation/ Melanin/Whitening

Introduction

In recent years, there is continuously increasing of Asian woman who aspire a whiter skin (Tengamnuay, Pengrungruangwong, Pheansri, & Likhitwitayawuid, 2006). Thus, whitening cosmetics become popular products and have high market value. Moreover, it leads to increase discovery of novel effective skin whitening agents. In general, Arbutin, Hydroquinone, Vitamin C and Kojic Acid are examples of whitening compounds that affect to tyrosinase inhibition and melanin synthesis reduction (Chang, 2009).

α -Bisabolol [1-methyl-4(1,5-dimethyl-1-hydroxhex-4(5)-enyl)-cyclohexen-1] is a monocyclic sesquiterpene alcohol extracted from German Chamomile (*Matricaria chamomilla*) (Figure 1). α -Bisabolol is known to possess anti-inflammatory, analgesic, and antibiotic properties (Lee, Jun, Jung, Ha, & Park, 2010). The combined α -bisabolol with ginger extract has the synergistic anti-irritant efficacy which was shown *in vivo* on detergent-induced erythema (Herrmann, Meyer, Joppe, & Vielhaber, 2007). Previous study reported that α -bisabolol was an effective inhibitor of hyperpigmentation by inhibiting α -MSH-induced melanogenesis (Kim et al., 2008). Moreover, α -bisabolol-containing cream has significant lightening effect in the pigmented skin of the Korean female subjects (Lee et al., 2010).

The aim of this study was to evaluate skin whitening efficacy of cream containing α -bisabolol in various concentration (0.1 – 1.0 %) in Thai volunteers. The whitening effect was studied on normal skin and hyperpigmentation skin. Non-invasive electrical instruments (Mexameter and Chromameter) were used to determine the melanin content and skin lightness after applications of the products.

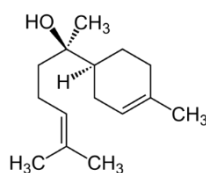


Figure 1 Structure of α -bisabolol

Objectives

1. To prepare whitening cream containing α -bisabolol
2. To study whitening efficacy of whitening cream in volunteers

Methods

Preparation of whitening product containing α -bisabolol

α -Bisabolol (99 %) was purchased from Citróleo, Brasil. Oil-in water cream was prepared which various concentrations of α -bisabolol (**Table 1**). Sun flower oil was mixed together with Polyacrylate-13 (and) Polyisobutene (and) Polysorbate 20 (Sepiplus 400) and DI water until homogenous. Next, glydant plus was added into the mixture. Finally, α -bisabolol was added into the mixture at concentration of 0.1, 0.5 and 1.0 %.

Table 1 List of ingredients of whitening product

Ingredient	Function	Amount (%w/w)			
		F1	F2	F3	F4
DI water	Diluent	91.7	91.6	91.3	90.7
Sun flower oil	Emollient	5.0	5.0	5.0	5.0
Seppiplus 400	Emulsifier	3.0	3.0	3.0	3.0
Glydant plus	Preservative	0.3	0.3	0.3	0.3
α -Bisabolol	Active	0.0	0.1	0.5	1.0

Stability test

The stability of whitening products (F1 – F4) were investigated by using heating-cooling cycles testing. The product samples were stored in hot air oven (45°C) for 24 hours, and then changed to store in refrigerator (4°C) for 24 hours (1 cycle). When finished 7 cycles of heating-cooling test, the product samples were observed for changes of texture, color, odor, separation, pH and viscosity.

Safety evaluation of whitening product

The whitening product safety was determined by skin primary irritation method using closed patch test on 15 volunteers. The patches were attached to the upper arm of volunteers for 24 hours which including F1 – F4 as test sample, 0.5 % sodium lauryl sulfate as positive control, and distilled water as negative control. Then, skin reactions were evaluated after 30 min, 24 and

48 hours of the patches test removing and scored the skin reaction values following **Table 2**. The score were completed by the calculation of the mean irritation index (M.I.I) according to the following equation. The interpretation of the calculated M.I.I scale is shown in **Table 3**.

The mean irritation index (M.I.I) = Sum of irritation grade/ number of subject

Table 2 Scoring of patch test reaction

Interpretation	Skin reaction	Score
Negative reaction	No erythema	0
Doubtful reaction	Very slight erythema	0.5
Weak positive reaction	Slight erythema	1
Strong positive reaction	Well-defined erythema	2
Extreme positive reaction	Moderate to severe erythema	3
Severe positive reaction	Beet redness and extending beyond area of exposure	4

Table 3 The Mean Irritation Index (M.I.I.)

M.I.I.	Class
M.I.I. < 0.20	No irritating
$0.20 \leq \text{M.I.I.} < 0.50$	Slightly irritating
$0.5 \leq \text{M.I.I.} < 1$	Moderately irritating
$\text{M.I.I.} \geq 1$	Irritating

Efficacy evaluation of whitening product

Fifteen healthy subjects, aged 20 – 40 years old were chosen for this study and were given to sign informed consent form. Volunteers were divided into two groups which were normal skin group (n = 10) and hyperpigmentation (n = 5). The hyperpigmentation was stimulated by exposure to UV source (30 watt) for 1 hour. The product was applied twice a day with F1 – F4 on upper arms for 4 weeks. The melanin content and skin color were measured at

week 0 and week 4 by using Mexameter (MX18, Courage&Khazaka, Germany) and Chromameter (CR-400, Konica minolta, Japan), respectively.

Statistical analysis

All the experimental data were expressed as means \pm SD. Statistical analyses were performed by ANOVA with SPSS program (SPSS Inc., Chicago, USA). A p-value of less than 0.05 was considered significant.

Results and Discussion

Preparation of whitening product containing α -bisabolol

In this study, O/W emulsion was developed by using DI water as diluent, sun flower oil as emollient, polyacrylate-13 (and) polyisobutene (and) polysorbate 20 (sepiplus 400) as emulsifier, and glydant plus as preservative. The prepared base emulsion was white glossy cream (**Figure 2**). α -Bisabolol was used as active ingredient and added into base emulsion at various concentrations (0, 0.1, 0.5 and 1.0 %). The appearance of each formula was similar and no separation after adding α -bisabolol. Moreover, the stability was evaluated by using heating-cooling condition for 7 cycles. The appearance, color, odor, pH and viscosity did not change over the test period.



Figure 2 Appearance of emulsion

Safety evaluation of whitening product

The safety of whitening product was determined by using skin irritation method (closed patch test) on upper arm of 15 volunteers for 24 hours. The 0.5% sodium lauryl sulfate was used as positive control and its M.I.I result was 1 that means irritating. While, the M.I.I result

of DI water (negative control) and whitening product containing α -bisabolol were 0 that means non irritant. (**Figure 3**)

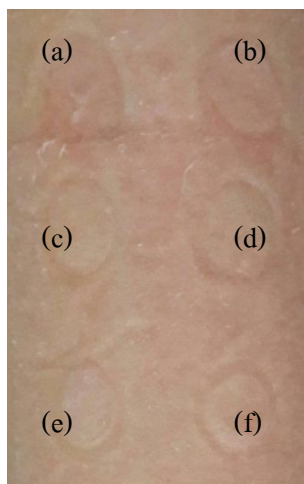


Figure 3 Appearance of tested skin after 24 hours patch test of (a) positive control, (b) negative control, (c) control whitening cream, (d) 0.1 % α -bisabolol cream, (e) 0.5 % α -bisabolol cream, and (f) 1.0 % α -bisabolol cream

Efficacy evaluation of whitening product

Fifteen healthy subjects, aged 20 – 40 years old were divided into three groups including normal skin type III-IV (n = 5), normal skin type V (n = 5), and hyperpigmentation (n = 5) classified by Fitzpatrick scale (Sachdeva, 2009). They applied the products on upper arms for 4 weeks. Then, the melanin content and skin color were measured by using Mexameter and Chromameter, respectively. The results were presented as change values of melanin index value and lightness value which calculated by comparing with the initial value.

Normal skin

After 4 weeks , the results in normal skin illustrated that emulsion with α -bisabolol at concentration of 1.0 % was able to significantly decrease the maximum melanin content about 28.6 ± 15.3 (P < 0.05) (**Table 1**) and increase the skin lightness at significant level 3.8 ± 1.7 (P < 0.05) (**Table 2**). The skin color of the volunteers before and after test are show in **Figure**

Table 1 Melanin index of normal skin in week 0 and week 4

Formula	week	Volunteers	Melanin index value		Sig. (p-Value)*
		(n)	w 0 - w 4		
			Δ Mean	SD	
Control cream	0	10	-38.1	27.6	0.035*
	4	10			
0.1% α -bisabolol	0	10	16.7	14.6	0.063
	4	10			
0.5% α -bisabolol	0	10	18.0	9.4	0.013*
	4	10			
1.0% α -bisabolol	0	10	28.6	15.3	0.014*
	4	10			

Note. Tested by One-Way ANOVA (95% Confidence Interval of the Difference)

*Significant (p -Value < 0.05)

Table 2 Lightness value of normal skin in week 0 and week 4

Formula	week	Volunteers	L* value		Sig. (p-Value)*
		(n)	w 0 - w 4		
			Δ Mean	SD	
Control cream	0	10	-1.7	2.9	0.263
	4	10			
0.1% α -bisabolol	0	10	2.6	0.7	0.001*
	4	10			
0.5% α -bisabolol	0	10	3.5	3.2	0.070
	4	10			
1.0% α -bisabolol	0	10	3.8	1.7	0.007*
	4	10			

Note. Tested by One-Way ANOVA (95% Confidence Interval of the Difference)

*Significant (p -Value < 0.05)

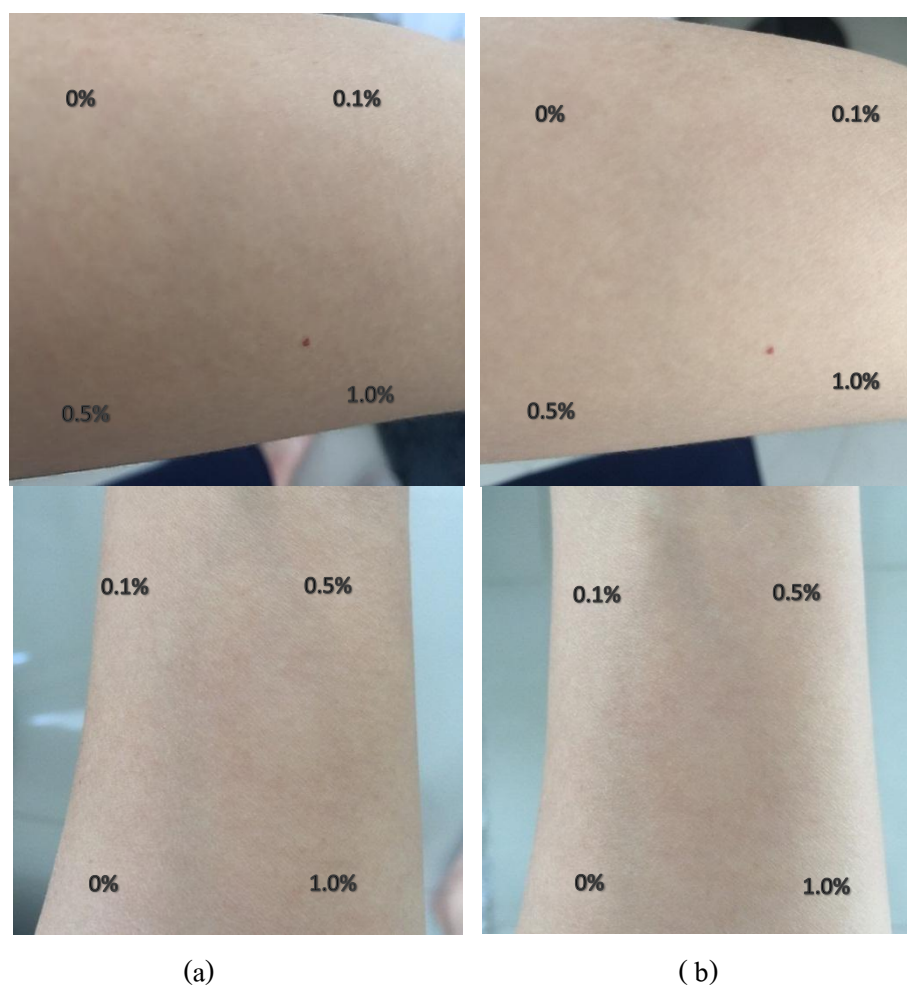


Figure 4 Appearance of skin color before tested skin (a) and 4 weeks after application (b) of normal skin group

Hyperpigmentation

After 4 weeks , the results in hyperpigmentation skin illustrated that emulsion with α -bisabolol 0.1 % were also able to significantly decrease the melanin content at significant level 19.8 ± 3.7 ($P < 0.05$) (**Table 3**) and increase the skin lightness at significant level 4.0 ± 1.5 ($P < 0.05$) by α -bisabolol at concentration of 0.5 % (**Table 4**). The skin color of the volunteers before and after test are show in **Figure 5**

Table 3 Melanin index of hyperpigmentation skin in week 0 and week 4

Formula	week	Volunteers	Melanin index value		Sig. (p-Value)*
		(n)	w 0 - w 4		
			Δ Mean	SD	
Control cream	0	5	-28.8	22.9	0.048*
	4	5			
0.1% α -bisabolol	0	5	19.8	3.7	0.000*
	4	5			
0.5% α -bisabolol	0	5	11.3	4.8	0.006*
	4	5			
1.0% α -bisabolol	0	5	13.2	6.6	0.011*
	4	5			

Note. Tested by One-Way ANOVA (95% Confidence Interval of the Difference)

*Significant (p -Value < 0.05)

Table 4 Lightness value of normal skin in week 0 and week 4

Formula	week	Volunteers	Melanin index value		Sig. (p-Value)*
		(n)	w 0 - w 4		
			Δ Mean	SD	
Control cream	0	5	-2.4	2.8	0.127
	4	5			
0.1% α -bisabolol	0	5	1.7	0.4	0.001*
	4	5			
0.5% α -bisabolol	0	5	4.0	1.5	0.004*
	4	5			
1.0% α -bisabolol	0	5	2.2	1.1	0.012*
	4	5			

Note. Tested by One-Way ANOVA (95% Confidence Interval of the Difference)

*Significant (p -Value < 0.05)

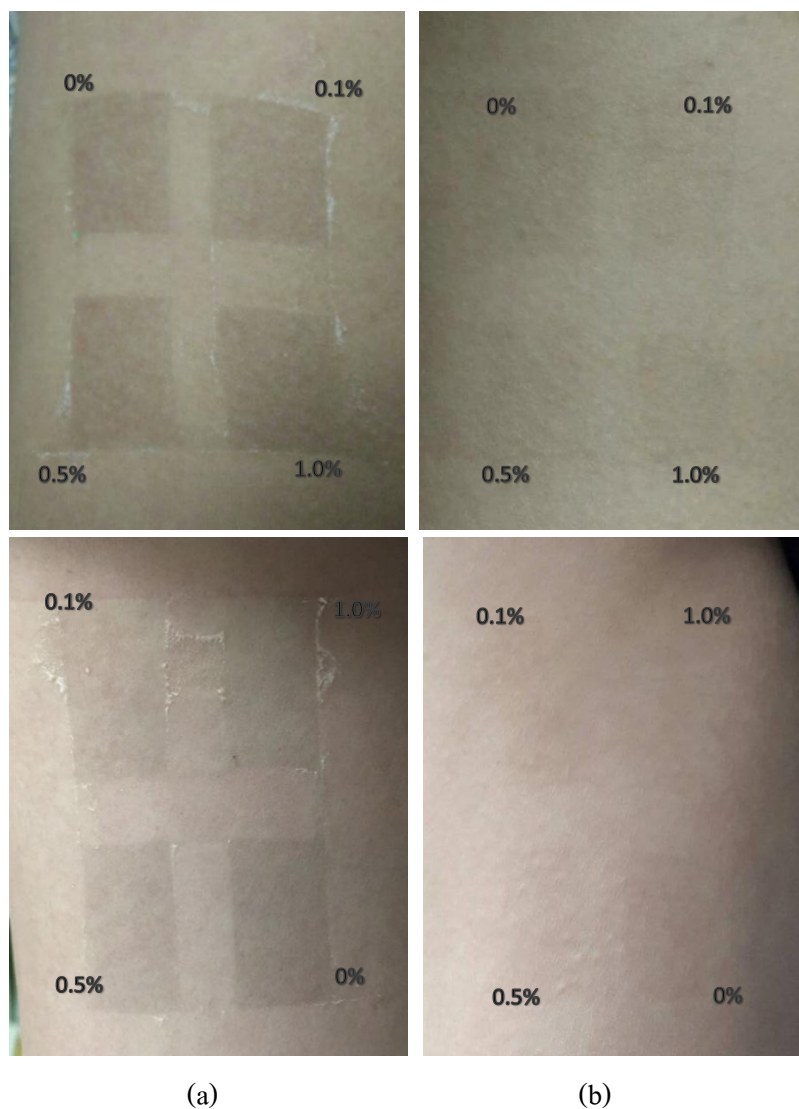


Figure 5 Appearance of tested skin before (a) and 4 weeks after application (b) of hyperpigmentation group

Conclusion

The whitening product containing α -bisabolol was prepared as oil-in-water emulsion. It had white glossy cream, good texture and good stability. In safety tests, there were no reactions in any volunteers, thus α -bisabolol cream was considered safe for use in volunteers. The effectiveness of 0.1, 0.5 and 1.0 % α -bisabolol was tested for 4 weeks on 15 volunteers. After 4 weeks of treatment, there was significant reduction in melanin content and increase in the lightness of skin color. The whitening cream contains α -bisabolol 1.0% can be effectively used

on the normal skin. While, the hyperpigmentation skin whitening cream that content 0.1- 0.5% α -bisabolol were recommended.

References

- Chang, T. S. (2009). An updated review of tyrosinase inhibitors. *Inter J Mole Sci*, 10, 2440-2475.
- Herrmann, M., Meyer, I., Joppe, H., & Vielhaber, G. (2007). The synergetic anti-irritant effects of (-)- α -bisabolol and ginger. *Cosmet Toilet*, 122, 79-86.
- Kim, S., Lee, J., Jung, E., Huh, S., Park, J.O., Lee, J.W., Byun, S.Y., & Park, D. (2008). Mechanisms of depigmentation by alpha-bisabolol. *J Dermatol Sci*, 52(3), 219-222.
- Lee, J., Jun, H., Jung, E., Ha, J., & Park, D. (2010). Whitening effect of α -bisabolol in Asian women subjects. *Inter J Cosmet Sci*, 32, 299–303.
- Sachdeva, S. (2009). Fitzpatrick skin typing: Applications in dermatology. *Indian J Dermatol Venereol Leprol*, 75, 93-96.
- Tengamnuay, P., Pengrungruangwong, K., Pheansri, I., & Likhitwitayawuid, K. (2006). *Artocarpus lakoocha* heartwood extract as a novel cosmetic ingredient: evaluation of the *in vitro* anti-tyrosinase and *in vivo* skin whitening activities. *Inter J Cosmet Sci*, 28, 269–276.