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ORIGINAL ARTICLE

The effect of 2% niacinamide on facial sebum production

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Abstract

Background: The presence of sebum on the face is responsible for both facial shine and the formation of comedonal and inflammatory acne lesions. Sebum control is a goal of many OTC skin care products; however, most currently available products function by absorbing sebum from the face rather than modulating its production. **Objective:** To demonstrate the effect of topical 2% niacinamide on sebum excretion rates and casual sebum production in Oriental and Caucasian populations. **Methods:** Separate clinical trials were conducted in both Japan and the USA to evaluate the effect of topical 2% niacinamide in different ethnic groups. A total of 100 Japanese subjects were enrolled in a double-blind, placebo-controlled comparison between two independent balanced groups. Fifty subjects applied the 2% niacinamide moisturizer to the face for 4 weeks and 50 subjects used a placebo moisturizer for 4 weeks, with sebum excretion rate (SER) measurements taken at baseline, week 2, and week 4. In addition, 30 Caucasian subjects were enrolled in a randomized split-face study for 6 weeks with SER and casual sebum levels (CSL) measured at baseline, week 3, and week 6. **Results:** The results of the Japanese study demonstrated that the SER of the two groups was not significantly different at baseline, but the 2% niacinamide treated group demonstrated significantly lowered SER after 2 and 4 weeks of application. The results were somewhat different in the Caucasian study. After 6 weeks of treatment, the CSL was significantly reduced, but the SER was not significantly reduced. **Conclusions:** Topical 2% niacinamide may be effective in lowering the SER in Japanese individuals and CSL in Caucasian individuals.

Key words: Sebum production, niacinamide, oily skin

Introduction

An important component of skin physiology is the thin film of lipids composed of triglycerides, diglycerides, fatty acids, wax esters, squalene, sterols, sterol esters and phospholipids known as sebum (1,2). Sebum is secreted by the sebaceous glands, which are most numerous on the face, with a density of 400–800 glands/cm² (2–4). The typical facial sebum film is greater than 4 µm thick (5). The physiologic significance of sebum is not completely understood, but several possible functions of sebum are proposed, including: (i) barrier protection, especially regulation of transepidermal water loss; (ii) protection against sunburn; (iii) maintenance of the skin biofilm; and (iv) delivery of antioxidants to the skin surface (6,7). While sebum may perform important functions, the presence of sebum on the face is considered unaesthetic, contributing to facial shine and imparting an unclean, greasy feel to the

skin. Sebum is also associated with acne and large pore size. A demographic worldwide study revealed that oily skin is a common concern of 70% of US women and 62% of Japanese women (Procter & Gamble corporate survey).

The dermatologic literature contains research citing a number of substances that have been investigated for their ability to reduce sebum, such as 13-*cis*-retinoic acid (8,9), spironolactone (10), topical erythromycin/zinc (11), and antiandrogens (12). However, these are prescription medications intended primarily to treat acne with a secondary intent of reducing sebum. We wished to investigate a substance that could be safely used in the OTC market as a cosmeceutical to reduce the presence of facial sebum. To accomplish this goal, we evaluated the effect of topical 2% niacinamide in two randomized, double-blind, clinical trials conducted among healthy Japanese and US females with excess

sebum production, since it is widely perceived that sebum control may differ ethnically.

Method

The test material consisted of a hydrophilic gel containing 2% niacinamide as the primary active and 1% *d*-panthenol as a humectant. The placebo consisted of the same hydrophilic gel, but without niacinamide or panthenol. The two gels were filled into identical opaque white bottles with metered pump dispensers to blind both the subjects and the investigators as to the identity of the contents. Two studies were undertaken to evaluate the effect of 2% niacinamide in both Oriental and Caucasian skin in Japan and the USA.

Japanese study

A total of 100 healthy Japanese female subjects, aged 20–49 years (mean age 36.4 ± 6.2 years), were successfully enrolled in the Oriental arm of the study following the completion of an informed consent. Subjects were selected based on their self-perception of skin oiliness. Fifty randomized Japanese subjects received a 2% niacinamide hydrophilic gel and the remaining 50 subjects received the placebo gel. The subjects were instructed to apply one squirt from the dispenser to the entire face twice daily for 4 weeks, which yielded approximately 45 g of product. Sebum production was evaluated on the forehead at baseline, week 2, and week 4 using both a Sebumeter (Courage Khazaka, Germany) and Sebutapes (CuDerm, USA). The Sebutapes were placed at symmetrical sites above the eyebrows following aggressive cleansing with 70% isopropyl alcohol and left on the skin for 45 minutes. The tapes were then detached and transferred to transparent slides for storage in a -20°C freezer until analyzed. Sebumeter readings were taken in triplicate from different locations on the center forehead immediately after 70% isopropyl alcohol cleansing and 90 minutes later. The sebum excretion rate (SER) was determined by the difference of the two readings. The environment of the test facility was maintained at $21 \pm 2^{\circ}\text{C}$ and $50 \pm 10\%$ ambient humidity throughout the study period.

Sebutapes were evaluated by illumination from a white LED source (KDB-25SLE(W), Kos System, Japan) and photography of the tape with a digital microscope (VH-8000, Keyence, Japan) to capture an 8 bit gray scale image. The translucency of the Sebutape was increased with sebum absorption, allowing increased light transmission and creating a geometric pattern of sebum production on the tape for computer analysis using Optimas 6.5 (Media Cybernetics, Inc., USA) (Figures 1 and 2). The software yielded an oil area fraction on the Sebutape

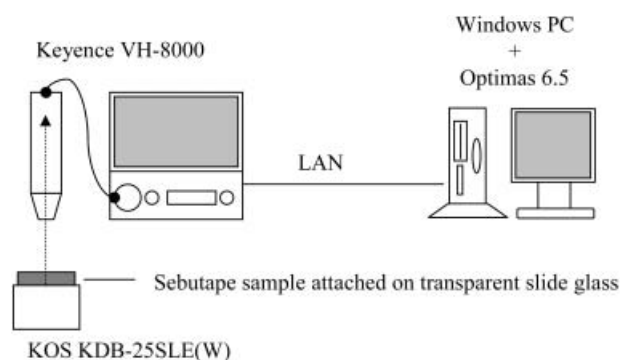


Figure 1. Sebutape Image Analysis System used in the Japanese study. The LED light source (KOS KDB-25SLE(W)) illuminates the Sebutape sample from the bottom. Light transmits more freely through the area where the Sebutape has absorbed sebum and turned translucent, while the original Sebutape is opaque allowing less light to pass through. The contrast highlights the sebum area on the Sebutape. The image is recorded and analyzed by computer-based software that recognizes the sebum area automatically, as shown in Figure 2.

that was defined as follows:

$$\text{oil area fraction [\%]} = \frac{\text{area of the tape where sebum was absorbed}}{\text{total adhesive area of sebutape}} \times 100$$

The duplicate Sebumeter and Sebutape measurements were averaged for each subject and the mean of the active and placebo groups at baseline, week 2, and week 4 were compared using Student's *t*-test with significance defined as $p \leq 0.05$.

US study

A total of 30 females, aged 20–49 years, were enrolled in the Caucasian arm of the study following completion of an IRB-approved informed consent (Schulman and Associates, Cincinnati, OH, USA). The enrollment criteria and the active study product were identical to the Japanese study arm; however, the US study was a split face design. Study subjects were instructed to apply the active study product to the randomized right or left face and leave the opposite side untreated. Sebum production was measured at baseline, week 3, and week 6 using a Sebumeter SM810 (Courage Khazaka), Sebutapes (Cortex, USA), and the dermatologist investigator's visual assessment. When subjects arrived at the test facility, their casual sebum level (CSL) was measured immediately using the Sebumeter. Subjects were then asked to wash their faces and their entire foreheads were scrubbed with 70% isopropyl alcohol by the research coordinator. Two Sebutapes were then placed on symmetrical sites above the eyebrows and left in place for 90 minutes in the controlled environment of the research center. The tapes were detached and read using a Sebutape optical analyzer to calculate the oil absorption based on translucency

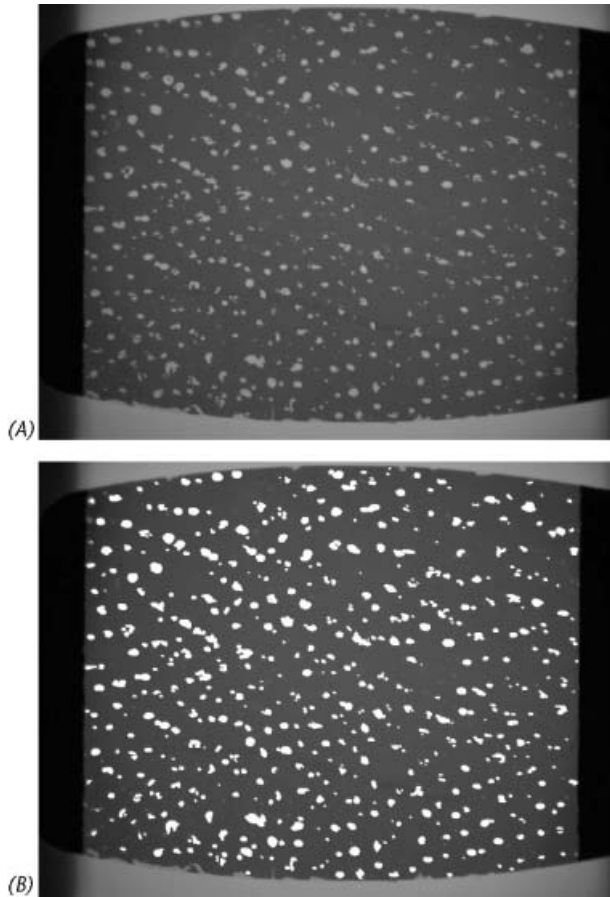


Figure 2. Image analyzed Sebutape. The original Sebutape image (A) and result of sebum area detection by the automated software (B; the sebum area is highlighted in white). Holes are counted when they are complete; the ones on the edge of the tape are not counted.

of the Sebutape (DermaLab, Cortex Technologies, Broomall, PA, USA). Sebumeter readings were taken in triplicate from different locations between the eyebrows immediately after cleansing and 90 minutes later. The SER was determined by the

difference in the two readings at 0 and 90 minutes. The dermatologist investigator's assessment was performed for overall facial skin condition, oiliness, and shine at baseline, week 3, and week 6.

An ANCOVA analysis was used to evaluate the Sebumeter and Sebutape data using the pretreatment sebum level as the covariate. The investigator assessment data were tabulated and analyzed using a Fisher's exact test with significance defined as $p \leq 0.05$.

Results

Japanese study

In all, 98/100 Japanese female subjects completed the 4-week study, with one subject experiencing a flare in facial acne. Two subjects discontinued for personal reasons. At the start of the study, there was no significant difference in the SER between the 2% niacinamide active and placebo groups. The SER decreased during the study for both the active and the placebo groups with both measurement methods (Table I). The 2-week Sebumeter-measured average reduction in sebum production in the 2% niacinamide group was 21.3% compared with 8.6% in the placebo group ($p=0.013$). At week 4, the Sebumeter-measured sebum reduction was 21.8% in the active group compared with 10.7% in the placebo group ($p=0.027$) (Figure 3). The Sebutape evaluations were directionally the same as the Sebumeter readings, but statistical significance between the control and placebo groups was not achieved at week 2. However, at week 4 the Sebutape-measured SER was reduced in the niacinamide active group over the placebo group ($p=0.011$) (Figure 4). Comparing the change from baseline at week 2, the niacinamide treatment group showed a statistically significant SER reduction over the placebo group in Sebumeter measurement

Table I. Sebum excretion rate of pretreatment and post-treatment (Japanese study).

	Treatment	<i>n</i>	Mean	SD	SEM	<i>p</i> -value
Sebumeter (90 min–0 min)						
Pretreatment	A	49	155.25	63.55	9.08	0.351
	P	49	166.91	59.48	8.50	
Week 2	A	49	122.05	58.16	8.31	0.013
	P	49	152.63	61.24	8.75	
Week 4	A	49	121.34	59.13	8.45	0.027
	P	49	149.07	63.41	9.06	
Sebutape						
Pretreatment	A	49	5.607	2.714	0.388	0.430
	P	49	6.110	3.524	0.503	
Week 2	A	49	4.741	2.313	0.330	0.395
	P	49	5.170	2.652	0.379	
Week 4	A	49	4.180	1.917	0.274	0.011
	P	49	5.372	2.595	0.371	

A=active; P=placebo. The Sebumeter (90 minutes of face wash) reading corresponds to micrograms per square centimeters and the Sebutape (45 minutes) reading is the % oil area fraction. The changes in Sebumeter and Sebutape readings are also visualized in Figure 3 and Figure 4, respectively.

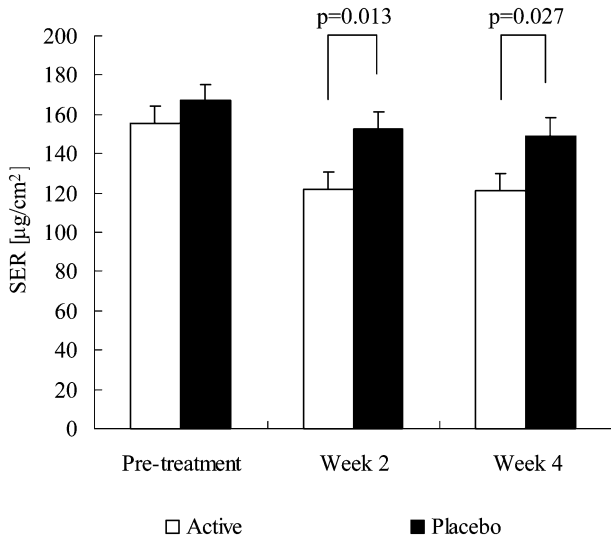


Figure 3. Sebum excretion rate (90 minutes measured using Sebumeter SM810): pretreatment and post-treatment (Japanese study). The SER of the active group was level with the placebo group before the onset of treatment. After 2 and 4 weeks of treatment using 2% niacinamide hydrophilic gel, the SER was significantly reduced compared with the placebo group. The error bar indicates the standard error of the mean.

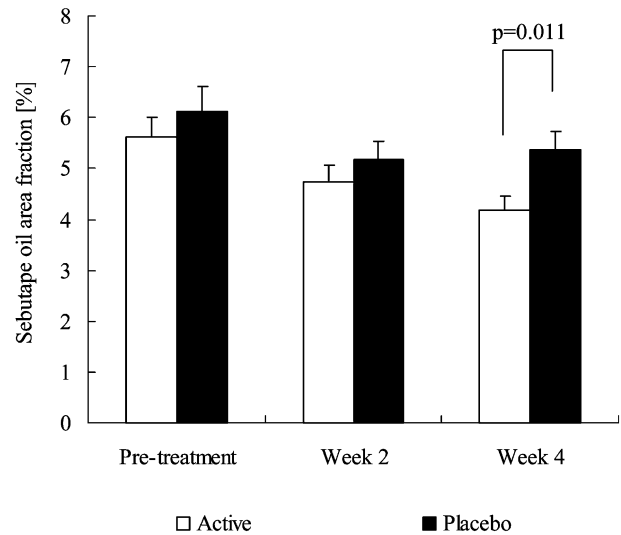


Figure 4. Sebum excretion rate (45 minutes measured using Sebutape): pretreatment and post-treatment (Japanese study). Sebumeter measurement showed that the SER of the active group was significantly reduced compared with the placebo group after 4 weeks of topical application of 2% niacinamide. The error bar indicates the standard error of the mean.

($p=0.024$), but statistical significance was not observed at week 4.

US study

All 30 Caucasian subjects completed the 6-week split face study without adverse events. In the Sebutape and Sebumeter analysis, no statistically significant differences were observed between the

niacinamide and the untreated control sites in SER at 3 and 6 weeks (Table II). Sebutape readings did not show a reduction compared to baseline; however, the Sebumeter showed directionally less sebum production on the treated versus untreated face. Statistical significance was not achieved because both the untreated and treated side of the face showed a sebum reduction from baseline, perhaps due to the greater attention to cleansing on the part of the subjects who knew they were being observed.

Table II. Casual sebum level and sebum excretion rate of pretreatment and post-treatment (US study).

	Treatment	N	Mean sebum level	Mean difference from pretreatment	Std. error	p-value
Casual sebum level						
Pretreatment	A	26	198.04	0.00	10.33	1.000
	U	26	198.04	0.00	10.33	
Week 3	A	29	179.48	-16.86	9.481	0.151
	U	29	191.19	-5.141	9.511	
Week 6	A	28	181.40	-14.93	9.618	0.055
	U	28	200.56	4.228	9.623	
Sebumeter (90 min-0 min)						
Pretreatment	A	26	189.27	0.00	12.75	1.000
	U	26	189.27	0.00	12.75	
Week 3	A	29	115.82	-65.20	11.43	0.219
	U	29	131.21	-49.81	11.50	
Week 6	A	28	137.18	-43.84	11.69	0.644
	U	28	142.99	-38.03	11.65	
Sebutape (sebum area %)						
Pretreatment	A	29	2.591	0.00	0.459	0.385
	U	29	2.024	0.00	0.459	
Week 3	A	29	3.659	1.400	0.899	0.915
	U	29	3.602	1.343	0.903	
Week 6	A	28	4.634	2.375	0.909	0.682
	U	28	4.411	2.152	0.907	

A=active; U=untreated.

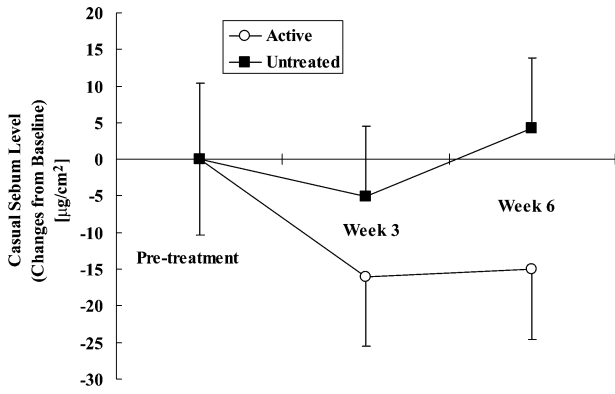


Figure 5. Change of casual sebum level from pretreatment (US study). The error bar indicates the standard error.

However, the CSL on the niacinamide-treated side of the face almost showed a statistically significant ($p=0.055$) reduction in sebum compared with the untreated side at week 6 (Figure 5).

The blinded dermatologist investigator was visually able to detect differences between the niacinamide and untreated sides of the face. There was a statistically significant reduction in facial shine at week 6 ($p=0.009$) and oiliness at week 3 ($p=0.024$) and week 6 ($p=0.0002$) with the niacinamide gel (Table III). In addition, there was a statistically significant improvement in facial skin appearance in the niacinamide-treated side of the face at both week 3 ($p=0.012$) and week 6 ($p=0.00001$).

Discussion

Many products are currently entering the cosmeceutical marketplace designed to reduce facial shine. Facial shine is in large part due to the layer of sebum that coats the skin surface. In certain cultures, such as the Orient, facial shine is considered undesirable and OTC sebum control products are rapidly entering the marketplace. This study was designed to critically evaluate the ability of 2% niacinamide to

reduce facial sebum production. The active agent was chosen as 2% niacinamide since it is considered safe and in vitro studies have demonstrated its ability to decrease sebum production (13). The study was conducted in Japan and the USA to evaluate the effect of niacinamide in two different ethnic populations while employing several recognized methods of sebum evaluation. The study conducted in Japan compared the placebo gel to the active gel containing niacinamide and panthenol while the US study compared one side of the face treated with the active gel with the untreated side of the face.

Two studies were performed because there is some controversy about whether sebum control studies should be placebo controlled or split face. One study cannot incorporate both designs. The placebo-controlled study can be faulted because there is no method of assessing what would have happened with no treatment and the split face design study can be faulted because cross contamination from the treated and untreated side of the face is a possibility. Sebum control studies are notoriously difficult to perform, since facial sebum appears to decrease just because subjects are enrolled in a study. This phenomenon is seen in all clinical dermatology research. Certainly, the decrease in facial sebum from baseline in both the placebo group in Japan and the untreated side of the face in the US study confirms this observation. This unexplained sebum decrease created problems in achieving statistical significance with several of the measurements.

Overall, the investigator assessment of visual sebum presence proved to be the most statistically significant. This is the advantage of a split face study where each subject can act as their own sebum production control. Differences in facial shine and oiliness with the active niacinamide were apparent. However, the cause of this reduction could be decreased production of oil by the sebaceous gland, a decreased reservoir of sebum in the follicular ostia, or absorption of the oil on the skin surface. Many different types of sebum measurements were

Table III. Improvement in visual skin condition change (Investigator’s Visual Assessment): US study.

	Overall facial skin condition				Facial shine				Oiliness			
	Week 3		Week 6		Week 3		Week 6		Week 3		Week 6	
Improved moderately	0	0	0	1	0	0	0	1	0	0	1	1
Improved mildly	83.33	16.67	94.12	5.88	75.00	25.00	77.78	22.22	73.68	26.32	79.17	20.83
No change	19	25	12	25	20	26	14	22	15	23	8	21
Worsen mildly	0	2	0	1	0	0	0	1	0	1	0	1
Total	29	29	28	28	29	29	28	28	29	29	28	28
P value	0.012		1.78E-05		0.103		0.009		0.024		2.86E-04	

collected as part of this study to determine the possible mechanism of sebum reduction.

The US study did not provide much statistically significant data in terms of Sebutape or Sebumeter readings even though there was a directional decrease with the use of the niacinamide gel. This could be due to possible cross contamination of the sides of the forehead where the readings were taken. The Japanese study, which was placebo-controlled, was better suited to evaluate the instrumental effect of niacinamide on the skin, since cross contamination was not possible. Thus, the Japanese study demonstrated a statistically significant reduction in both Sebutape and Sebumeter readings at week 4. Since sebum production at the sebaceous gland level is under hormonal control, it is unlikely that the niacinamide gel reached the sebaceous gland to alter sebum production. There were also no ingredients in the niacinamide or placebo gels that could absorb sebum to the degree demonstrated. It is theorized that the niacinamide possibly altered the movement of sebum to the skin surface by altering the reservoir in the duct connecting the sebaceous gland to the skin surface at the follicular ostia. Niacinamide has been previously demonstrated to induce enhanced exfoliation of the skin surface (14). It is theorized that the same exfoliation occurred within the duct and encouraged sebum to flow to the skin surface more quickly. This depletion of the reservoir eventually translated into decreased sebum excretion on the skin surface. However, continued use of the niacinamide would be necessary to keep the reservoir depleted and maintain the decreased surface facial sebum.

This research demonstrated the potential use of 2% niacinamide and 1% *d*-panthenol for facial shine reduction. It is possible that a moisturizer using these ingredients might aid in an improved cosmetic appearance for both Oriental and Caucasian individuals. Further characterization of the mechanism of action of niacinamide in oil reduction is warranted.

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