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"Niacinamide and N-Acetyl Glucosamine (NAG) Moisturizing Gel on Indonesian Teenagers' Skin"

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1. Introduction

Generation Z, people born in 1996-2012, will make up a quarter of the population of Asia-Pacific (APAC) region by 2025, combining with Millennials (born between 1981 to 1996), both generations will constitute half of APAC population [1]. This demographic shift will make Generation Z an important consumer for future beauty industries [2]. Growing up during global COVID-19 pandemic period made Generation Z develop their own characteristics in terms of their skincare habits, thanks to their longer exposure to their phones and internet. In most countries, Generation Z spend two hours more than Generation X and one hour longer than Millennials on their phones, this made Generation Z unique as they tend to spend more time in research before they purchase a skincare product [1]. High exposure to social media also increases the awareness of Generation Z of what their skin needs and what kind of skincare products have the solution for their problems [2].

Generational Z tends to perceive their skin as more sensitive and prone to acne and redness [3]. This could be explained by the fact that majority of Generational Z is currently undergoing or just finished adolescent period, in which hormonal change and lifestyle influence tends to affect skin condition. High levels of androgens in adolescent girls can create a hypersensitive sebaceous gland, producing high sebum production on skin [4]. Excessive sebum provides a nutrient-rich environment for the proliferation virulent *C. acnes* and the development of comedones, thereby starting the acne vulgaris pathogenesis. *C. acnes* colony will develop into biofilm which the skin will fight using various inflammatory responses. However, skin inflammation will produce acne bump, erythema (redness), and if not treated can lead to post-inflammatory hyperpigmentation (PIH) [5].

Acne vulgaris is one of the most common dermatological conditions affecting adolescents worldwide [6]. Acne affects approximately 85% of individuals aged 12 to 24 years, with varying

degrees of severity, making it a significant public health concern in this demographic. Besides acne, oily skin in teenagers can create an appearance of dull skin, another most common skin problem for teens [7]. Environmental pollutants can induce oxidative stress and inflammation in the skin, aggravating acne [8]. These environmental and lifestyle factors further aggravate acne problems in teens and Generation Z.

One of the prevalent strategies to treat acne vulgaris and skin pigmentation is using Niacinamide as the main active ingredients in skincare regime due to its multifunctional benefits. Niacinamide can prevent the transfer of melanosome from melanocytes to the keratinocytes, thus reducing the cutaneous pigmentation [9]. Niacinamide also proved to reduce the production of sebum on the skin and contribute to the reduction of inflammation in acne vulgaris [10][11]. Due to its benefit and affordable price, Niacinamide is becoming more popular and found in many mass-market products which some of it is marketed towards teenagers and Generation Z who has lower purchasing power compared with older and more matured consumers.

Several other skincare ingredients have been studied to complement Niacinamide in treating skin problems. One of the ingredients is N-acetyl Glucosamine (NAG), an amino hexose known as precursor of hyaluronic acid. NAG showed anti-melanogenesis activity, reducing the production of melanin in melanocytes [12]. Its polymeric structure also makes NAG an important ingredient for the structure and moisturization of skin cells extracellular matrix [13]. Their difference of chemical structure and biological mechanism in skin, makes NAG a promising ingredient to be combined with Niacinamide for the treatment of skin problems in teenagers. Clinical trials of Niacinamide and NAG have already been conducted in older panelist (40-60 years old) to evaluate the reduction of hyperpigmentation [12]. This study aims to evaluate the combination of Niacinamide and NAG as an effective treatment for teenager skin problems.

2. Materials and Methods

Preparation of Niacinamide & NAG Moisturizing Gel

We developed Niacinamide 4% and NAG 2% moisturizing gel with the following ingredients: Aqua, Niacinamide, Acetyl Glucosamine, Betaine, C13-15 Alkane, Propanediol, Ammonium Acryloyldimethyltaurate/VP Copolymer, Hydroxyacetophenone, Arachidyl Alcohol, Synthetic Fluorphlogopite, Allantoin, Bisabolol, Jojoba Esters, Behenyl Alcohol, Chlorphenesin, Propylene Glycol, Arachidyl Glucoside, Polyacrylate-13, Fragrance, Polyisobutene, Glycerin, Polysorbate 20, Tin Oxide, Sodium Chloride, Sodium Ascorbyl Phosphate, Phenoxyethanol, Trideceth-9, PEG-40 Hydrogenated Castor Oil, Ethylhexylglycerin, CI 77891, and CI 17200.

Safety Test

Product safety was evaluated by Single Patch Test (SPT) and Human Repeat Insult Patch Test (HRIPT) SPT was conducted over a period of 9 days for 30 subjects. Product was placed under occlusive patch for duration of 24 hours on the upper back of the subjects. Patches were

then removed and skin reaction was assessed 30 minutes and 24 hours post removal using Draize Scale.

HRIPT consisted of four phases, namely induction phase, rest phase, challenge phase, re-challenge phase (selective). Repeated application of a test product was performed on the back of the subjects, under occlusive patch for duration of 24 hours. Product was applied three times a week for a total of nine applications. All assessments were performed 48 hours post patch application. Following a two week rest period. After the rest period, a 24-hour challenge application of each material was made. The evaluation was done at 48, 72, and 96 hours post patch application.

Efficacy Test

Product efficacy was evaluated in 38 healthy female subjects aged 17 - 23 years old with all skin types and uneven skin tone. The subjects were asked to apply the formula twice daily for 28 days. Assessment of skin parameters' improvement related to dark spot, visible pores, and sebum level was conducted using instrumental measurements (spectrophotometer), image analysis, visual assessments by a dermatologist, and a self-assessment questionnaire. In this study, the dermatologist also observed the cutaneous reaction to prove the formula's safety.

3. Results

Safety test

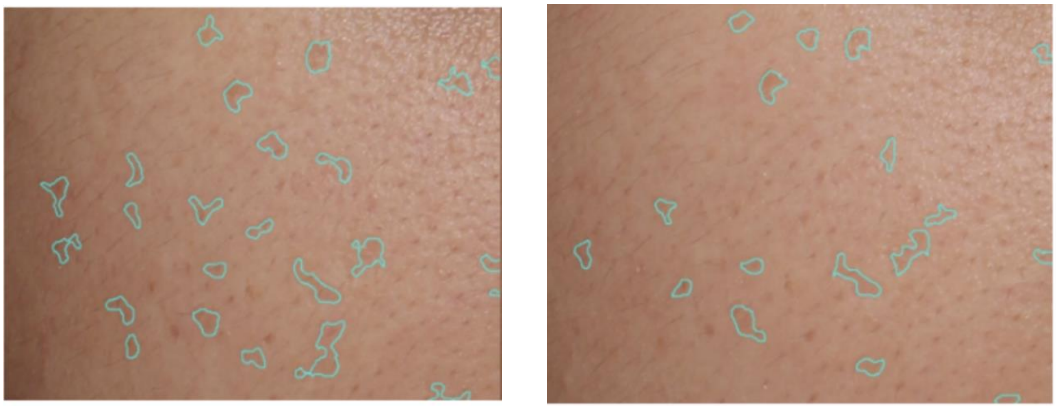
SPT and HRIPT results proved the gentleness of the formula on skin by showing non-irritating and hypoallergenic results. These findings were further supported by dermatologist assessment during the in vivo study, which proved the formula to be non-comedogenic, non-acnegenic, with no significant unwanted adverse events from cutaneous reaction observed.

Dark Spot and Skin Brightness

Table 1 shows a comprehensive evaluation of dark spot intensity and skin brightness levels assessed using multiple instruments and dermatologist observation. Colorimeter, Chromameter, and Antera 3D result showed significant increases in dark spot values, with changes of +7.76%, +1.13%, +1.30% respectively. Skin brightness level was evaluated by dermatologist in cheek area and dark spot area showed significant change with value -0.05% and -10.82%.

Table 1. Dark spot and skin brightness level measure by instrument at Day-28

Parameter Measured	Instrument	Result
Darkspot	Colorimeter	+7.76% ($p<0.05$)
	Chromameter	+1.13% ($p<0.05$)
Skin Brightness	Antera 3D	+1.30% ($p<0.05$)
Skin Brighteness Level (Cheek Area)	Dermatologist	-0.05% ($p<0.05$)
Skin Brighteness Level (Dark Spot Area)	Dermatologist	-10.82% ($p<0.05$)

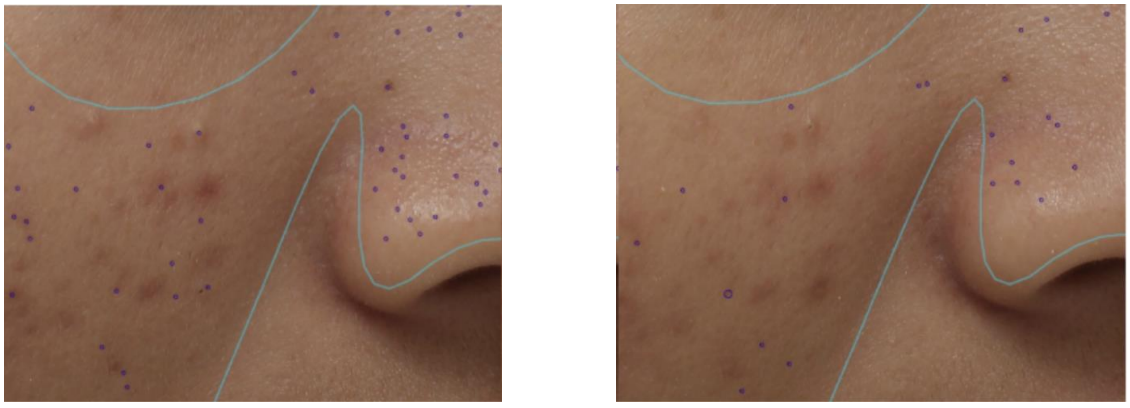


(a) (b)

Figure 1. Dark spot reduction measured by Visia Skin Analysis at (a) Day-0; (b) Day-28

Pore Appearance

After 28 days of usage, pore appearance improvements were noticed by reduction of area and diameters of pores measured by instrumental and image analysis (-5.63%, $p<0.05$, respectively). Moreover, visual assessment by dermatologist also showed reduction in pores visibility by -13.04% ($p<0.05$).



(a) (b)

Figure 2. Image Pro Analysis for pore reduction measurement at (a) Day-0; (b) Day-28

Sebum Level

79% of subjects reported that the formula was able to reduce skin sebum level after 28 days of usage.

Skin redness related to PIE/Blemish Skin

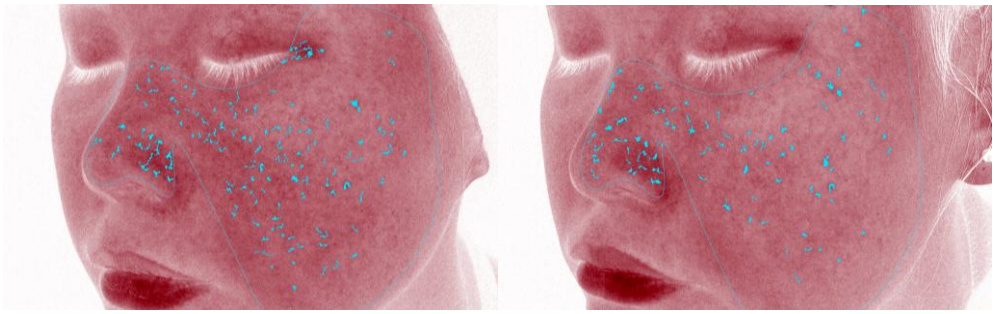
After 28 days of usage, erythema related to PIE and blemish skin was reduced significantly by instrumental measurements. Reduction in skin erythema was observed using the Mexameter (-7.82%, $p<0.055$), while skin redness levels also decreased as measured by the Colorimeter (-4.44%, $p<0.055$) and Antera 3D (-4.35%, $p<0.05$). Hemoglobin index also declined by -6.60% ($p<0.05$), indicating reduced vascular redness. The consistent findings indicate that the

combination of Niacinamide and NAG effectively reduces skin redness associated with PIE and blemished skin, as proven by multiple measurement methods.

Table 2. Erythema level evaluation by instrument

Parameter Measured	Instrument	Result
Erythema	Mexameter	-7.82% ($p<0.05$)
Redness	Colorimeter	-4.44% ($p<0.05$)
Redness	Antera 3D	-4.35% ($p<0.05$)
Hemoglobin Index	Spectrophotometer	-6.60% ($p<0.05$)

Figure 3 shows erythema spot reduction observed using redness filter in the Canfield Visia Gen 6. The blue spots, identified as erythema, help visualize the reduction in erythema over the 28-day period. Fewer blue spots at Day 28 indicate that the treatment effectively reduced erythema compared to the baseline at Day 0.



(a) **(b)**

Figure 3. Erythema spot reduction visualized using redness filter in the Canfield Visia Gen 6 at (a) Day-0; (b) Day-28

4. Discussion

This moisturizing gel was proven to brighten skin, dark spots, and pore appearance in teenager skin. Due to the combination of niacinamide and NAG in the moisturizing gel, it showed significant improvement of skin brightness, particularly the reduction of dark spot area by –10.82% in 28 days. This significant result could be explained by synergistic mechanism of niacinamide and NAG in skin brightening. While niacinamide acts at the latter stage of skin pigmentation by preventing the transfer of melanosome from melanocytes to keratinocytes, NAG with their glucosamine group will inhibit the glycosylation of tyrosinase and prevent the activation of tyrosinase, one of the first key steps in melanogenesis [14]. The dark spots reduction results found in this study will resonate with teenagers who periodically got hyperpigmentation spots due to acne marks.

The combination of niacinamide and NAG also significantly improve pore appearance in terms of the reduction of pore size and area. Niacinamide itself has known to have pore refining benefits which postulated comes from its ability to inhibit sebum production [15]. While the

mechanism of niacinamide in controlling the sebum production is not yet specifically determined, it is theorized that niacinamide changes the movement of sebum from the sebaceous gland to the surface of the skin. Since niacinamide can enhance the exfoliation of the skin surface, the same exfoliation mechanism could apply to the duct connecting the sebaceous glands with skin surface, encouraging faster flow of sebum to the surface of the skin. The depletion of sebum and emptying of sebaceous duct eventually translated in the reduction of skin sebum and the decrease of pore size that previously holding the sebum [10][16].

New findings in this study is the ability of the moisturizer with the combination of niacinamide and NAG in reducing skin redness due to post inflammatory erythema (PIE) and blemish skin. Previously, niacinamide was known to have a risk in creating skin flushing, due to the presence of niacin as the impurities of niacinamide. Niacin activated the hydroxycarboxylic acid receptor 2 (HCA2 or GPR109A) which will start a signaling cascades that will release prostaglandin which causes vasodilation in the skin, resulting in redness appearance on the skin [17]. However, the combination of niacinamide and NAG in this study did not creates skin flushing effect, but to the contrary it reduce skin redness appearance significantly.

5. Conclusion

The combination of niacinamide and NAG, formulated in the form of moisturizer could significantly tackle teenager skin problems by significantly improve skin brightness, reduce dark spot size, pore volume and area, skin sebum level, and erythema level related to PIE and skin blemish. Niacinamide and NAG could be the alternative of affordable skin care solutions for teenagers due to their inexpensive formulation cost, compared to other active ingredients.

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