IFSCC 2025 full paper (IFSCC2025-1579)

# *"N-Acetyl Glucosamine and Nonapeptide-1 as the Next Affordable, Promising Skin Brightening Agents for the Asian Market"*

**Yani Rahmawati[1], Margareta Anindya Christianti [1], Juang Arwafa Cita [1], Hira Listya Pinastika [1], Fransisca Hie [1]**

[1]Research and Development, Paragon Technology and Innovation, Tangerang, Indonesia

## 1. Introduction

Skin hyperpigmentation issues such as skin dullness, melasma, post-inflammatory hyperpigmentation, solar lentigines affecting individuals across age groups in Asian population [1]. Among the various active ingredients to target hyperpigmentation, niacinamide was wildly used in every skincare brightening product due to its proven efficacy and affordability. It has been recognized as a skin whitening agent by inhibiting 35–68% of melanosome transfer from melanocytes to keratinocytes [2]. In clinical studies, 2–5% niacinamide has been shown to be effective in reducing hyperpigmentation and increasing the L* value of the skin [3].

Beyond its brightening efficacy, niacinamide also exerts many functions. Niacinamide is an essential component of nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine phosphate (NADP). NAD and NADP are involved in cellular catabolism and anabolism processes, playing an essential role in cellular energy, supporting biosynthesis, and antioxidant function [4]. Niacinamide could support skin barrier health by inducing ceramide and cholesterol synthesis in the epidermis, increasing the synthesis of involucrin, filaggrin, and keratin (proteins related to the skin barrier), and protecting the skin from pollution, blue light, and UV-induced DNA damage [5–9]. Niacinamide can improve acne skin conditions, as shown by a 52% reduction in acne severity and a 60% reduction in the number of pustules and papules after 8 weeks of 4% niacinamide gel application. It also reduces the sebum excretion rate by 23% ($p < 0.05$) after 8 weeks and decreases pore size by 9.0% ($p < 0.05$) after 4 weeks of treatment with 2% niacinamide topical application [5,10]. Lastly, topical treatment with 2–5% niacinamide can increase collagen synthesis, thereby improving skin texture, wrinkles, and fine lines [3,4].

However, because of its popularity, the Asian skincare market is already saturated with niacinamide claims. Many manufacturers and consumers are seeking a new ingredient that could replace niacinamide but has the same potential as brightening agent. This is due to the formulation limitations of niacinamide, which can limit its application in certain product types, such as its tendency to crystallize at high concentrations and the complexity of formulations containing multiple powdered active ingredients or other raw materials that require high water content for solubilization [11]. In addition to formulation considerations, niacinamide raw material

contains niacin impurities, which can induce flushing in individuals with sensitive skin [12]. These factors highlight the need for alternative brightening agents that can provide comparable clinical outcomes to niacinamide while offering improved formulation flexibility and low irritation potential.

In recent years, N-Acetyl Glucosamine (NAG) and Nonapeptide-1 are recently gaining popularity as brightening ingredients. Both actives show potential in addressing hyperpigmentation through different mechanisms, but there was only a few evidence about their clinical efficacy [13, 14]. Therefore, this study was conducted to evaluate the safety and brightening effectiveness of NAG and Nonapeptide-1 compared to Niacinamide, thus providing additional scientific support for their potential use in cosmetic formulations.

## 2. Materials and Methods

### Preparation of Niacinamide, NAG, Nonapeptide-1 Moisturizing Gel

Chassis formulations were prepared by using the following ingredients: Aqua, Butylene Glycol, Glycerin, Ammonium Acryloyldimethyltaurate/VP Copolymer, Propanediol, Dimethicone, 1,2-Hexanediol, Chlorphenesin, Polyglyceryl-3 Methylglucose Distearate, Polysorbate 20, Carbomer, Disodium EDTA, Aminomethyl Propanol, and Caprylhydroxamic Acid. The tested active ingredients were incorporated into these formulations, such as Niacinamide 5%, NAG 2%, or Nonapeptide-1 0.0005%.

### Safety Test

Product safety was evaluated by Single Patch Test (SPT). 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.

### Efficacy Test

Product efficacy was evaluated in healthy female subjects aged 17 to 22 years, with all skin types and uneven skin tone. Participants were instructed to apply the formula twice daily for 28 days. The subjects were divided into two groups: Group 1 (27 subjects) was instructed to apply the moisturizing containing NAG and Nonapeptide-1 in split-face method, Group 2 (30 subjects) applied the moisturizing containing Niacinamide and served as the control group. Skin improvements were assessed through visual evaluation by a dermatologist, focusing on parameters such as skin brightness level and erythema levels, as well as through a self-assessment questionnaire. The dermatologist also monitored for any cutaneous reactions to evaluate the safety of the formula.

## 3. Results

### Safety Test

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

**Skin brightness level**

Skin brightness was evaluated by dermatologist assessments and subject self-assessment questionnaires. Dermatologist assessment showed that all formulations significantly improved skin brightness after 28 days of application. Niacinamide demonstrated the most significant reduction in brightness level, with a mean change of −16.72% ($p < 0.05$). This was followed by NAG at −12.65% ($p < 0.05$), and Nonapeptide-1 at −11.54% ($p < 0.05$). Self-assessment questionnaires showed different results. NAG and Nonapeptide-1 achieved statistically significant brightness reductions (-11.97% and -11.7%; $p < 0.05$), Niacinamide 5% produced a non-significant change (+0.52%). This variation highlights the potential disconnect between clinical evaluation and perceived effectiveness among different treatments.

**Table 1.** Skin brightness level measurement on Day-28 by dermatologist assessment and panelist questionnaire

| Formulation | Dermatologist Assessment | Self-Assessment Questionnaire |
|---|---|---|
| Niacinamide 5% | -16.72% (p<0.05) | +0.52% (ns) |
| NAG 2% | -12.65% (p<0.05) | -11.97%(p<0.05) |
| Nonapeptide-1 0.0005% | -11.54% (p<0.05) | -11.70%(p<0.05) |

**Skin erythema level**

Table 2 shows that Niacinamide achieved the highest reduction in erythema at 21.45%, followed by NAG at 7.38%, and Nonapeptide-1. All formulations demonstrated statistically significant improvements in reducing erythema, highlighting their potential effectiveness in addressing skin redness.

**Table 2.** Skin erythema level measurement after 28 days application of product

| Formulation | Erythema (Mexameter) |
|---|---|
| Niacinamide 5% | -21.45% (p<0.05) |
| NAG 2% | -7.38% (p<0.05) |
| Nonapeptide-1 0.0005% | -6.95% (p<0.05) |

## 4. Discussion

This study investigates the brightening efficacy and safety of two emerging skincare actives, NAG and Nonapeptide-1, and compares it with Niacinamide, one of the popular ingredients for skin brightening in Asian skincare products. Several studies have been conducted that demonstrate the significant brightening efficacy of NAG and Nonapeptide-1, and their popularity have risen in cosmetics formulations due to their competitive price index. Since NAG and Nonapeptide-1 act differently than niacinamide in brightening the skin, both ingredients could be an alternative or complementary to Niacinamide.

NAG, an amino hexose known as precursor of hyaluronic acid, works at the beginning of melanogenesis by inhibiting the glycosylation of tyrosine thus preventing the activation of tyrosinase in the melanocytes. NAG also modulates several skin pigmentation-related gene expressions, providing a multifaceted approach to the reduction of melanin production [14]. On the other hand, Nonapeptide-1 is a synthetic peptide derived from arginine, lysine, methionine, phenylalanine, proline, tryptophan, and valine. It works as a biomimetic peptide, competing and antagonizing α-MSH at the MC1-R receptor, effectively preventing the downstream activation of tyrosinase and subsequent melanin synthesis [15].

NAG and Nonapeptide-1 showed significant skin brightening efficacy after 28 days, but both still fall behind Niacinamide as the control of this study, based on dermatological assessment. Interestingly, subjective perception of panelist showed a noticeable difference, with the panelist did not noticing significant brightening improvement on their skin. On the other hand, formula with NAG and Nonapeptide-1 gives significant and noticeable improvement for the panelist, -11.97% and -11.7% respectively. This finding is important because consumers tend to be more satisfied with efficacy result that can be perceived and directly felt by the consumer [15].

These findings suggest that NAG and Nonapeptide-1 are promising brightening ingredients to be used as alternatives or in combination with niacinamide in skincare formulation. There were no significant adverse clinical signs recorded throughout the study, supporting the safety profile of both ingredients. Further studies with larger populations, dose-response concentrations, longer study periods, and comparison with another active ingredients would prove the efficacy and provide additional insights. Additionally, exploring another efficacy for NAG and nonapeptide-1 could help to maximize their cost benefit in future skincare products.

## 5. Conclusion

This study demonstrated that N-acetyl glucosamine (NAG) and Nonapeptide-1 are safe and effective brightening agents. It showed significant improvements in skin brightness after 28 days of use. While the efficacy result was slightly lower compared to niacinamide, NAG and Nonapeptide-1 provided noticeable improvements perceived by participants, highlighting their potential to enhance consumer satisfaction. These findings support the use of NAG and Nonapeptide-1 as promising alternatives or complementary agents to niacinamide in skincare formulations.

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