Topical N-Acetyl Glucosamine Provides Fast Acne-Reducing Benefits and Mildness Demonstrating Its Potential Utility in Enhancing Conventional Rx or OTC Acne Treatments

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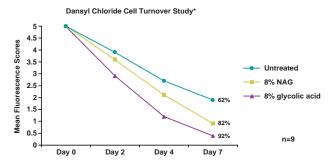
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Introduction

N-acetylglucosamine (NAG) is a chemically-neutral, amino sugar found in human proteoglycans and glycosaminoglycans (GAGs), including hyaluronic acid. ¹² Studies have shown that exogenously supplied NAG can stimulate the synthesis of water-binding GAGs by fibroblasts and keratinocytes, ³⁵ thus providing a basis for its use in anti-aging skincare. An anti-aging study of NAG revealed valuable cosmetic effects including diminished mottled pigmentation, improved skin clarity, and increased skin firmness and elasticity with a corresponding increase in skin thickness, so-called plumping.⁶

Other research has shown that NAG interacts with glycoproteins involved in corneocyte binding and intercellular cohesion, ^{7,8} and that topical NAG can reduce skin flakiness, increase dansyl chloride cell turnover rates, and normalize stratum corneum exfoliation. ⁹ Investigation into the exfoliative effects of NAG prompted a pilot cell turnover study. An abbreviated model was used to stain inner forearm skin with dansyl chloride. ¹⁰ NAG (8% cream, native pH 4.9) was compared to glycolic acid (8% cream, pH 3.7) and to an untreated control. NAG significantly reduced mean fluorescence scores compared to untreated (82%, 62% respectively), which was not as effective as the glycolic acid control (92%). NAG enhanced cell turnover rate and desquamation.

NAG Enhances Cell Turnover



- ➤ NAG increased cell turnover compared to untreated at each timepoint; p≤0.05
- *Abbreviated model used dansyl chloride (5% in petrolatum) was applied 3 hours under occlusion. Degree of fluorescence was evaluated using a Wood's lamp in a darkened room.

As a result of its ability to modify exfoliation, keratinization¹¹ and skin clarity,⁶ NAG was evaluated for its ability to influence mild to moderate acne for potential future use as an enhancing agent in anti-acne formulations.

Objective

This poster presents clinical study results demonstrating benefits to acne and skin clarity achieved by using the mild exfoliant NAG (8%, gel) in comparison to a control treatment, 10% Benzoyl Peroxide (BP) cream, to evaluate NAG's potential use as an adjunctive agent in acne therapy

Study Conduct

- Design: prospective, double-blind, positive controlled study with direct-comparison to baseline scores as well as between treatment comparisons for lesion counts and irritation parameters; protocol received IRB approval and informed consent was executed
- Subjects: males and females, 13-29 years of age with mild to moderate acne on the face (defined as 6-20 inflamed lesions and 10-100 non-inflamed lesions)
- Product Application: each group applied the assigned test product, either 8% NAG gel (pH 7.8) or 10% BP cream (commercially available), twice daily to their entire face
- Clinical Evaluations
- Lesion Counts and Clinical Grading (weeks 0, 1, 2, 4, 8): the number of papules, pustules, open comedones, closed comedones, as well as a global assessment of acne were assessed by a trained evaluator
- Irritation/Safety Grading (weeks 0, 1, 2, 4, 8): global evaluation of objective irritation and safety was conducted for dryness, erythema, peeling and roughness and subjective irritation scores were collected for burning, stinging, itching, tightness and tingling.
 Scale: 0 – 3 (none, mild, moderate, severe)
- Digital Photography (weeks 0, 4, 8) was collected using standardized lighting and positioning
- Self-Assessment (weeks 0, 1, 2, 4, 8) was collected via questionnaires

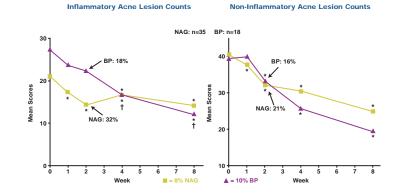
Statistics

- > Lesion counts, clinical grading and irritation grading
- For each group separately, mean values were compared to baseline scores using a paired $\emph{t\text{-}}\text{test}, p{\le}0.05$
- The two groups were compared to each other using ANOVA with Fishers LSD for pair-wise comparisons, $p{\le}0.05\,$
- Self-assessment questionnaires were tabulated and a top box analysis was performed

Results

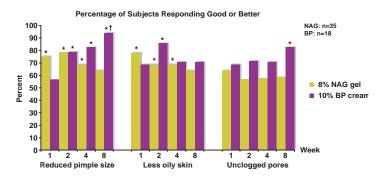
- 53 of 62 subjects completed the study; 35 subjects in the NAG group and 18 subjects in the BP group
- The 9 subjects that discontinued from the study were for reasons unrelated to the test products; 5 subjects in the NAG group and 4 subjects in the BP group

one Results



- NAG significantly reduced both inflammatory and non-inflammatory lesions beginning at week 1 and continuing over the 8 week treatment period; *p≤0.05
- > BP significantly reduced inflammatory lesions at week 4 and week 8, and non-inflammatory lesions at weeks 2, 4, and 8: *p≤0.05
- > BP was significantly more effective than NAG for inflammatory lesions at week 4
- Data for the global assessment of acne support the lesion count data in showing significant improvements from baseline for both NAG and BP, with BP becoming significantly more improved than NAG at weeks 4 and 8 (not shown)

Self-Assessment of Acne Skin Quality



Some early improvements are seen with NAG whereas BP's effect are evident at later time points; *top box analysis for each product, *difference between products. p<0.05</p>







Baseline 4 weeks 8 week
➤ 8% NAG gel reduces papules and improves skin clarity and inflammatory pigmentation

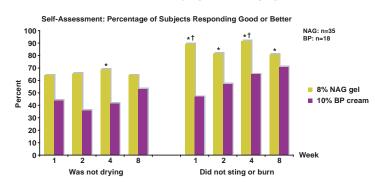
Skin Tolerability

NAG Gel is Significantly Better Tolerated vs. BP Cream

	Week 1	Week 2	Week 4	Week 8
Dryness	-	-	NAG	-
Erythema	NAG	-	-	-
Peeling	NAG	_	_	-
Burning	NAG	NAG	_	-
Stinging	-	-	NAG	NAG

- NAG is significantly better tolerated vs. BP on those parameters noted. A dash (-) indicates no significant difference between the products
- > There were no significant differences at any time point between the products for roughness, itching, tightness or tingling

NAG is Less Drying, Less Stinging



Self-assessment reveals the mildness characteristics of NAG and further supports the clinical grading for irritation; *top box analysis for each product, ¹NAG milder than BP, p≤0.05

Baseline



8% NAG gel improves skin texture and reduces pre-existing skin dryness, irritation and ervthema

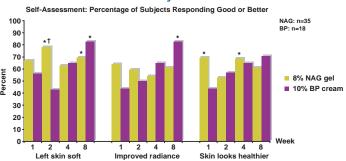


> 10% Benzoyl Peroxide cream increases erythema

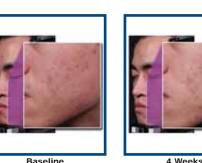
Baseline

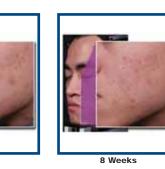
Cosmetic Benefits

NAG Provides Early Cosmetic Benefits



- NAG provides cosmetic benefits to skin health, radiance and softness most notably at the early timepoints; *top box analysis for each product, ¹NAG more improved than BP, p≤0.05
- > Favorable BP results take longer to achieve





> 8% NAG gel improves skin texture and clarity

Summary

N-acetyl glucosamine provides important anti-aging benefits to skin including exfoliation, skin smoothing and GAG-building/plumping without irritation. This study demonstrates that NAG's benefits extend to skin with acne, providing early cosmetic and therapeutic benefits to skin when compared to a mainstay in topical acne therapy, 10% Benzoyl Peroxide. The summary of findings in this study include:

- NAG quickly reduced the number of acne lesions showing good effects within the first 2 weeks and continuing over the 8 week treatment period
- > The early benefits of NAG were outperformed by BP for lesion counts at the later timepoints (weeks 4 and 8)
- > NAG statistically outperformed BP for skin tolerability and mildness parameters
- Self assessed cosmetic advantages were noted with NAG early in the study for radiance and softness

Combination use of NAG with topical anti-acne therapeutic agents could provide: (1) enhanced cosmetic benefits to acne skin, (2) enhanced therapeutic effect of an active agent, and/or (3) improved tolerability of active ingredients. Further investigation into specific combinations is warranted.

References

- Ebling FJG, Eady RAJ, Leigh IM. Anatomy and organization of human skin. In: Champion, Burton and Ebling, Eds fifth edition. Textbook of dermatology. Oxford: Blackwell Scientific Publications. 1992;88-90.
- Yu RJ, Van Scott EJ. Hydroxycarboxylic acids, N-acetylamino sugars, and N-acetylamino acids. SKINmed 2002;2:117-122.
- Sayo T, Sakai S, Inoue S. Synergistic effect of N-acetylglucosamine and retinoids on hyaluronan production in human keratinocytes. Skin Pharmacol Physiol. 2004;17:77-83.
 Breborowicz A, Kuzlan-Pawlaczyk M, Wieczorowska-Tobis K, et al. The effect of N-acetylglucosamine as a sub
- strate for in vitro synthesis of glycosaminoglycans by human peritoneal mesothelial cells and fibroblasts. *Adv Perit Dial.* 1998;14:31-35.

 5. Osborne R, Mullins L, Robinson L. Topical N-acetyl qlucosamine and niacinamide increase hyaluronan in vitro.
- J Am Acad Dermatol. 2006;54:AB106.
 6. Green BA, Edison BL, Wildnauer RH, Hwu RH. Derivatives of Sugar Compounds Provide Anti-Aging Effects.

 Amer Acad of Dermatol Poster Exhibit: Washington, DC, February 2004.
- Brysk MM, Rajaraman S, Penn P, et al. Glycoproteins modulate adhesion in terminally differentiated keratinocytes. Cell Tissue Res. 1988;225:657-665.
- Hudson DL, Sleeman J, Watt FM. CD44 is the major peanut lectin-binding glycoprotein of human epiderm keratinocytes and plays a role in intercellular adhesion. J Cell Science. 1995;108:1959-1970.
- 9. Presented at 23rd IFSCC Congress: Orlando, FL, October 2004.
- 10. Data on file, NeoStrata Company, Inc., 2004
- 11. US Patents 6,159,485; 6,524,593

Poster exhibit at the 65th Annual American Academy of Dermatology Meeting:
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