

Niacinamide

A Multifunctional Vitamin for a Complete Beauty Regimen



INCI Name:
Niacinamide

Key Niacinamide Benefits

- Helps replenish essential skin lipids to help protect skin barrier function.
- Helps balance the skin microbiota.
- Helps mitigate the effects of UV and environmental pollutants.
- Helps reduce the appearance of fine lines and wrinkles.
- Helps brighten and rebalance uneven skin tone.
- Helps to reduce the appearance of blemishes.
- Helps to improve dry and oily scalp condition.
- Manufactured using a green chemistry process¹.

What is Niacinamide?

Niacinamide (nicotinamide) comprises one of the two forms of Vitamin B₃; niacin (or nicotinic acid) being the other, both of which provide equivalent vitamin activity. As an essential component of living cells, Vitamin B₃ is essential for protein, carbohydrate and fat metabolism. Niacinamide is a precursor in the synthesis of the pyridine coenzymes NAD and NADP involved in cell metabolism, and as such play a key role in the production of energy.

Lonza – Your Reliable Supplier for Niacinamide

Lonza has been a leading supplier of Vitamin B₃ [niacin] for over 50 years, producing it in different forms for the dietary supplements, food, personal care, pharma and animal nutrition markets.

Lonza has over 25 years of experience in manufacturing Niacinamide, allowing it to produce material that meets the highest standards of quality and consistency. The Lonza Niacinamide, nature identical compound, is manufactured following a ISO14001 certified process, and designed to minimize impact on the environment.

Product Description:

Consumers of facial skincare products, and the formulators developing those products, have an abundance of choices of active ingredients to achieve the specific skin benefits they are seeking. These ingredients cover a very wide range, from pure compounds to natural extracts representing complex and often poorly defined chemical mixtures. The majority of these ingredients carry little recognition with consumers, which, in part, is due to the market's constant thirst for new and exciting ingredient technologies.

When it comes to the efficacy of these ingredients, in the vast majority of cases, it is largely unclear exactly what they bring to the table. This is because often clinical evidence of efficacy is based on *in vitro* studies alone, or when *in vivo* studies are presented, they lack placebo formulations or positive controls.

There are a number of consumer trends, both in the cosmetic space and adjacent categories, that signal a shifting approach of consumers towards cosmetic ingredients. First, there is an increasing demand for ingredients of natural origin, as well as finished products that are sustainable and contain fewer ingredients. Second, today's better informed consumer appears to have more faith in ingredients they are already familiar with, rather than the "latest and greatest." The latter trend has led to a renaissance of "tried and true" skincare ingredients, as evidenced by the recent explicit callout of ingredients like retinol, vitamin C, and glycolic acid in advertising.

One particular class of ingredients that has enjoyed increasing attention and acceptance from consumers is that of vitamins, for a number of reasons that reflect the core of these ongoing trends. For one, they are a naturally occurring class of ingredients, where there is close to universal acceptance of the link between their oral intake and general body health. Second, for a number of vitamins, including vitamin A (retinol), vitamin B₃ (niacinamide), vitamin B5 (provitamin panthenol), vitamin C (ascorbic acid), and vitamin E (tocopherol), a large body of scientific literature exists documenting their specific skin benefits.^{2,4}

Out of these, niacinamide should be on the top of any formulator's list

to include as an active ingredient in virtually any skincare product. Niacinamide has a number of important skincare benefits, including skin brightening, skin barrier improvement, reduction in the appearance of wrinkles and fine lines, and soothing properties⁵⁻⁶ (Fig. 1). And while many vitamins suffer from issues of chemical instability and skin irritation (especially retinol), that can make them challenging from a formulation/manufacturing perspective, niacinamide is highly stable, easy to formulate with, and well tolerated by the skin up to use levels as high as 10%.^{7,8}

Lonza has over twenty-five years of experience in manufacturing niacinamide, allowing it to produce material that meets the highest standards of quality and consistency. The Lonza Niacinamide, nature identical compound, is manufactured following eleven of twelve green chemistry principles.¹ The process is ISO14001 certified, and designed to minimize impact on the environment. The biocatalyzed process from the starting API material utilizes only water as solvent, which is safe and reduces waste. Biocatalysis provides high selectivity and high conversion rates. Exothermal energy is recovered, thus saving energy.

Niacinamide is now accompanied by a new technical data set, offering numerous new insights into the skin efficacy of niacinamide and its mechanisms of action, providing skincare brands with multiple new marketing angles.

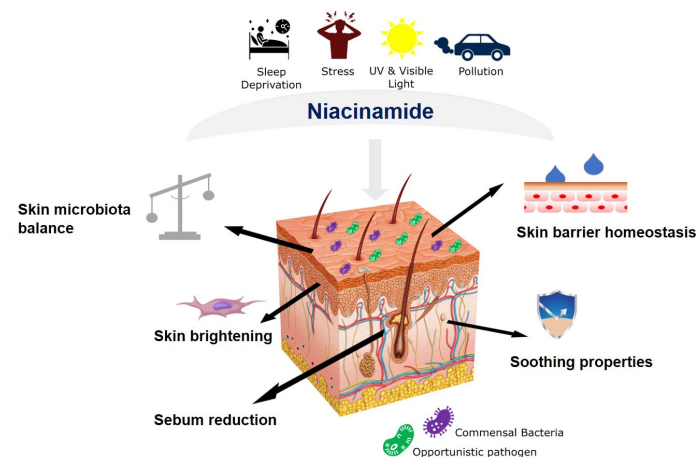


Figure 1: Schematic of the multifunctional benefits of niacinamide^{7,8}.

Skin Benefits of Niacinamide

Vitamin B₃, in the form of niacinamide, is one of the most widely studied topical skincare ingredients. Numerous peer-reviewed studies have revealed its many benefits on the skin, which include clinically proven efficacy to brighten the skin, reduce appearance of fine lines and wrinkles and soothing properties as well as enhancing the skin barrier and rebalancing the skin's microbiota. Because of this wealth of scientific evidence, it should come as no surprise that niacinamide is widely used in the cosmetic field in a variety of different products addressing a multitude of skin concerns. Good skin tolerability and ease of formulation further contribute to the widespread use of niacinamide.

Niacinamide continues to be studied extensively, with new benefits and insights into its mode of action being reported on a regular basis. Below, we summarize some of the key benefits of niacinamide, while presenting some exciting new data.

1. Brightening and Evening Skin Tone

Niacinamide reduces the amount of melanin produced by cultured normal human melanocytes and in a 3D tanned epidermis model (Fig. 2). The amount of melanin is reduced by 18% - 22% in cultured melanocytes after 5 days incubation with niacinamide (Fig. 2a), a similar decrease to that observed in the presence of the positive control, 0.01% kojic acid, assayed in the same experiment.

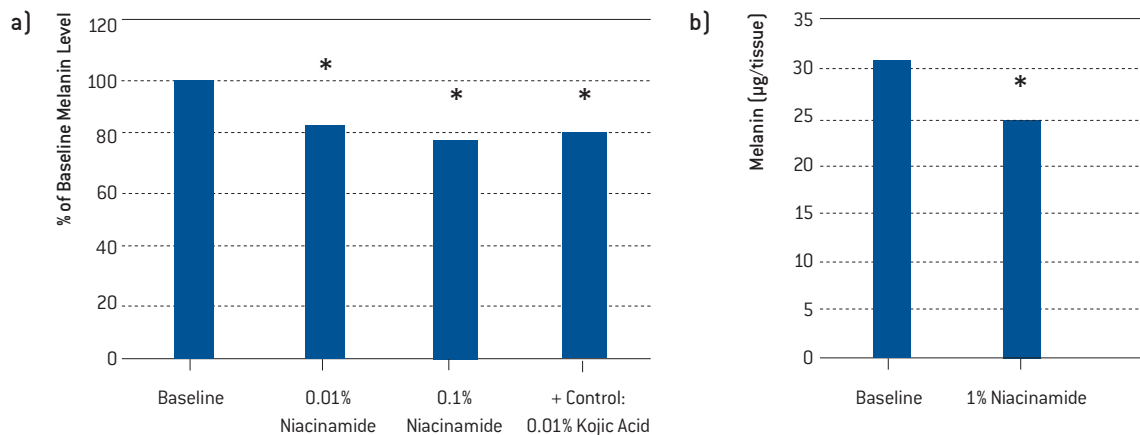


Figure 2: Melanin synthesis assays in vitro. (a) Melanin synthesis in cultured melanocytes after 5 days incubation with or without niacinamide. Results were confirmed in cells from two different donors. Significance assessed using t-test with * $p < 0.05$. (b) The 3D model [SkinEthic™ RHE] was tested in triplicate, with a 1% topically applied niacinamide solution. Significance was * $p < 0.05$.

A statistically significant reduction of 19%, vs baseline expression, was obtained during a 9-day study where 1% niacinamide was incubated with a tanned epidermis model (Fig. 2b). The higher dose of niacinamide required to elicit a clinical response is reflective of the product being applied topically to a 3D skin model, where the bioavailability is more similar to that *in vivo*.

Experiments by Mi *et al.* showed that 0.06% niacinamide, added in media for 6 days, was able to almost completely mitigate the skin darkening effect of the environmental pollutant, benzo[*a*]pyrene (BaP), applied topically to a 3D skin model, composed of keratinocytes and melanocytes, for 3 days.⁹ They also observed an effect of niacinamide on PMEL protein expression, suggesting that melanosome transfer from melanocytes to keratinocytes is the mode of action for the reduction in melanin content (Fig. 3), confirming what has been suggested by other researchers.¹⁰⁻¹¹

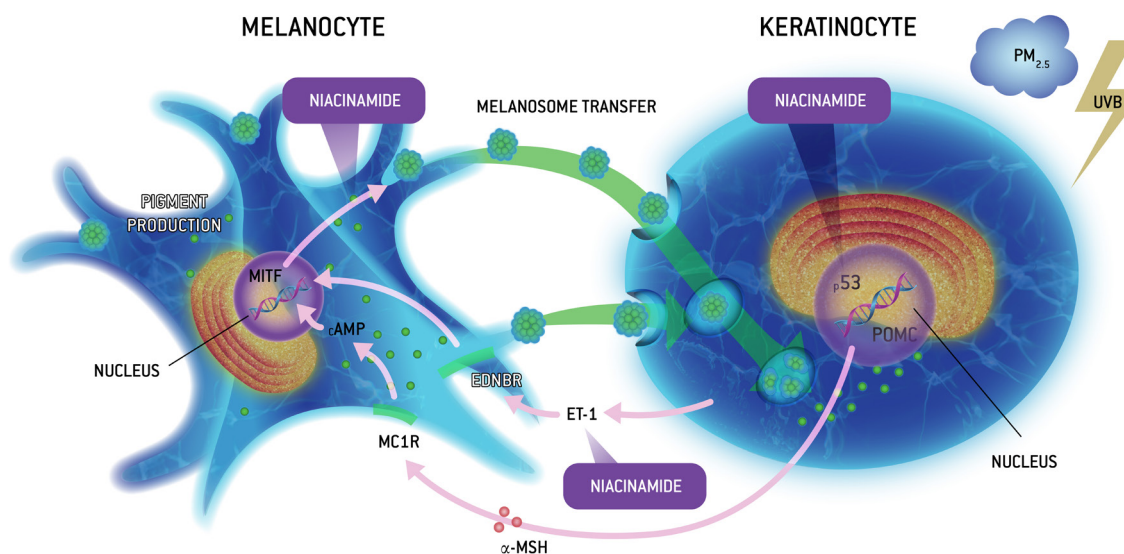


Figure 3: Communication between keratinocytes and melanocytes governs melanin production and distribution. Figure adapted from H. Ando *et al.*¹² and J.A. Lo and D.E Fisher¹³

In addition to inhibiting melanosome transfer, niacinamide has also been reported to interfere with the initiation of melanin synthesis regulated by messenger molecules, α -MSH and endothelin-1, secreted by keratinocytes. *In vitro* experiments revealed that niacinamide returned gene expression levels of p53, a key marker in suntan response and hyperpigmentation disorders¹⁴ to baseline levels, following application of the environmental fine particle pollutant, PM_{2.5} (SRM 2786). Furthermore, niacinamide reduced the endothelin-1 protein level expressed by cultured keratinocytes, in the presence or absence of UVB exposure (Fig. 4). In the absence of UVB, endothelin-1 protein levels decreased by ~60% after incubation with 0.1% niacinamide, for 24 hours (Fig. 4a). Exposure of cultured cells to 30 mJ/cm² UVB caused endothelin-1 levels to increase, with levels dropping slightly below baseline in the presence of 0.1% niacinamide (Fig. 4b). Collectively, the data presented illustrate the multiple modes of action exhibited by niacinamide *in vitro* to regulate pigmentation.

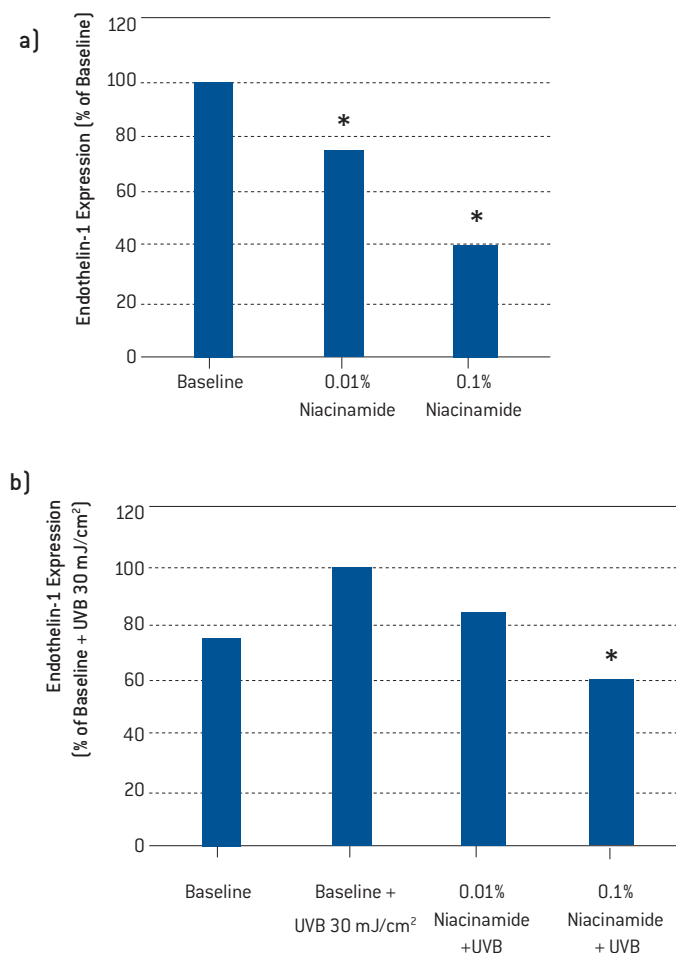


Figure 4: Endothelin-1 protein expression in cultured keratinocytes, in the absence (a), or presence (b) of UVB exposure. Data shown are the result of experiments with keratinocytes from two different donors. Significance is considered when $*p < 0.05$.

Multiple *in vivo* studies have shown that niacinamide in topical formulations, can reduce the appearance of brown spots and balance uneven skin tone. In a double-blind, split face study on Asian women, Hakozaiki et al. reported a 73% reduction in apparent spot area after application of a 5% niacinamide-containing moisturizer for 8 weeks.¹⁰ Navarrete-Solis et al. reported a double-blind, split face study with Hispanic women, where they observed a similar level of reduction in pigmentation after 8 weeks, as determined by image analysis, from a 4% niacinamide formulation compared to a 4% hydroquinone formulation, and melanin content from biopsies was also reduced after niacinamide application. Further, the niacinamide formula was better tolerated.¹⁵

2. Skin Barrier Improvement

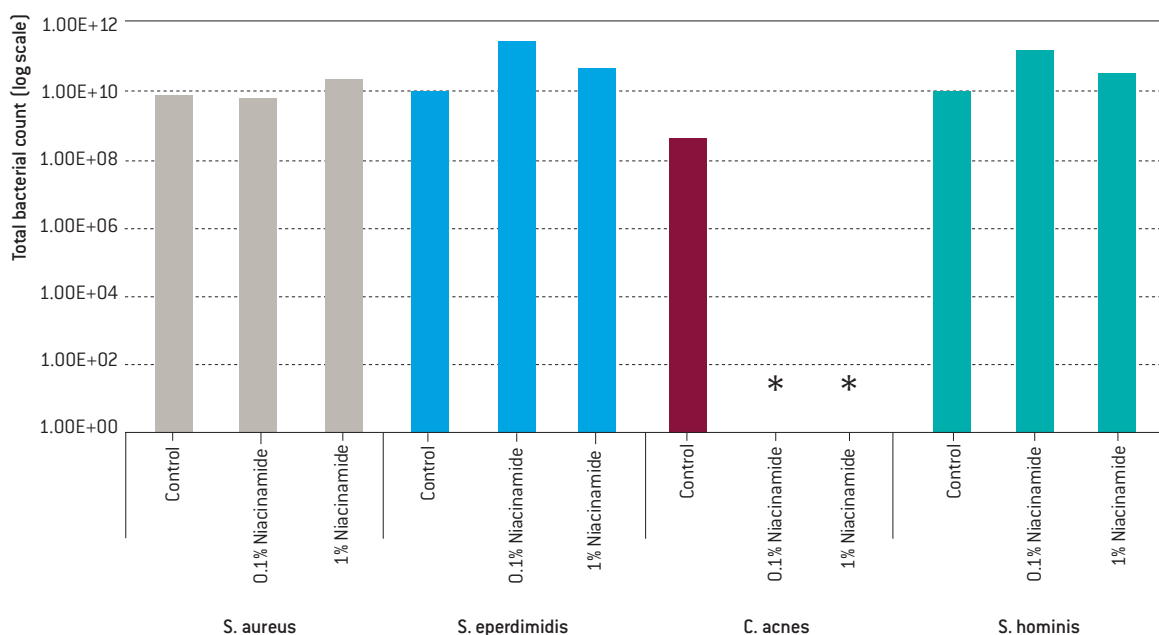
It is well documented that the quality of the skin barrier is of critical importance to the visual appearance and general health of the skin, as well as providing an effective shield against entry of exogenous compounds and species to the body. *In vitro* experiments have demonstrated a positive effect from niacinamide on the expression of multiple proteins critical to forming and maintaining the skin barrier, including filaggrin, involucrin, and keratin 1.^{8,16} Furthermore, niacinamide has been shown to improve the lipid composition of the epidermal barrier, by increasing the amount of sphingolipids produced by normal human keratinocytes *in vitro*. Following a 6 day incubation with 0.00012% niacinamide, significantly increased amounts of ceramide [2.9-fold], glucosyl-ceramide [7.3-fold], and sphingomyelin [3-fold] over baseline levels were observed in keratinocytes. In a 4-week transepidermal water loss (TEWL) study the same authors demonstrated a 27% decrease in TEWL and a 34% increase in ceramide content from a 2% niacinamide formula relative to a control formulation, suggesting a causal relation between the *in vitro* increases in protein expression and lipid production and the *in vivo* observation of barrier improvement.¹⁷ Another indicator of skin barrier condition is stratum corneum thickness with a thicker upper layer of the epidermis generally corresponding to a stronger barrier. In a double-blind study with healthy volunteers (aged 21-28 years) comparing a 5% niacinamide formula to control, a 10% increase in stratum corneum thickness and lower TEWL values compared to control, were observed on the forearm after twice daily application for 4 weeks.¹⁸

3. Maintaining the Skin Microbiota Balance

There is a growing interest, among both academic researchers and those in the beauty category, in the microbiota present on the skin. It has been proposed that the balance of different species present may be of critical influence to skin health. More specifically, a misbalance between commensal bacteria populations and opportunistic pathogens has been associated with different skin conditions such as blemishes, flaky skin, itch, oily skin, and malodor.¹⁹⁻²³

To model the mixed microbial populations found naturally on the skin, multiple bacterial species can be co-cultured *in vitro*. This model can then be exposed to cosmetic ingredients, and the response can be quantified by monitoring the viability of each microbial species in the model. Addition of niacinamide to this model revealed an effect of this molecule for *C. acnes*, and little to no effect on the other two commensal species present, *S. epidermidis* and *S. hominis* (Fig. 5). While *C. acnes* is also a commensal bacterial species, studies have found that strain identity and an imbalance in proportion of this species relative to others, has been linked to visible changes in skin appearance.

Figure 5: Total count of viable *S. aureus*, *S. epidermidis*, *C. acnes*, and *S. hominis* following a 48 hour incubation in the presence or absence of niacinamide. Each sample is an average of triplicates. * denotes significance versus the *C. acnes* control sample ($p < 0.05$).



While much of the ongoing research focuses on how external conditions and topical formulations, including probiotic approaches, affect that balance,²⁴ the skin itself maintains balance by producing antimicrobial peptides. A recent study offered fascinating insights in how niacinamide can help maintain a balanced skin microbiota, and strongly suggesting the stimulation of the skin's own ability to produce antimicrobial peptides as a mode of action.²⁵ In this study, formulations containing niacinamide (1% and 3%) as well as control formulation were applied to the forearm of healthy subjects.

After 6 hours, the impact on pathogenic bacteria and an antimicrobial peptide were measured. A significant decrease in *S. aureus* and *E. coli* was observed, as well as a 40% increase in the amount of the antimicrobial peptide, psoriasin. The increase in psoriasin was confirmed in cultured keratinocytes *in vitro* by gene expression, as were increases in the expression of additional antimicrobial peptides, RNase 7 and calprotectin.

The findings from those studies are consistent with reported efficacy of niacinamide in reducing the appearance of blemishes through the twice daily application of a 4% niacinamide gel, with the efficacy skewed towards subjects with oily skin.²⁶⁻²⁷ Furthermore, a moisturizer with 2% niacinamide was able to reduce sebum excretion rates after 4 weeks, compared to a control.²⁸ Based on the overall skin benefits, niacinamide may also have beneficial effects for scalp conditions,²⁹ where the skin barrier is compromised, but this application has not been extensively explored. In summary, the numerous skin benefits of niacinamide, in combination with the *in vitro* and *in vivo* studies providing insights into its mechanisms of action, make it the perfect ingredient for a variety of skin and scalp care formulations, providing excellent efficacy but also a variety of technical marketing angles. Specifically in light of consumer and market trends favoring known, nature identical ingredients produced based on green chemistry principles, Niacinamide should be the active ingredient of choice for both formulators and marketers.

In-Use Properties

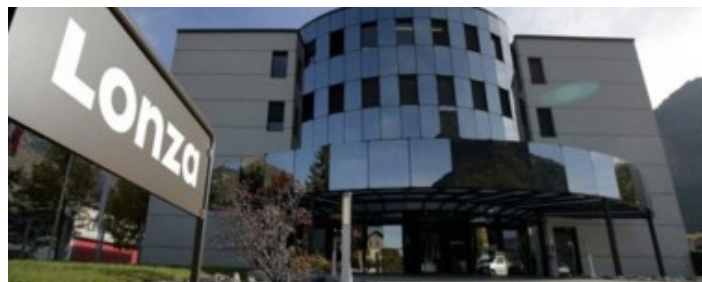
- Suggested Concentration: 1 - 5%
- Water soluble
- Easy to use
- pH stability: 4.5 - 8.0

Available Niacinamide Grades		
	Niacinamide USP PC	B3 Fresh™
CAS #:	98-92-0	
INCI:	Niacinamide	
Appearance:	Crystalline powder	
Color:	White	
Assay (HPLC):	99.0 – 101.0 %	
pH:	6.0 – 7.5 (5g/100 mL water)	
Heavy metals:	≤ 20 mg/kg (as Pb, limit test)	
Nicotinic acid:	≤ 200 ppm	≤ 100 ppm
SAP Code #:	202937	253235

- Readily biodegradable (OECD 301E)
- USP compliant
- Shelf life: 36 months

References

1. Anastas, P & Eghbali, N [2010] Green Chemistry: Principles and Practice. *Chem Soc Rev* 39:301-312.
2. Pullar, JM *et al.* [2017] *The Roles of Vitamin C in Skin Health*. *Nutrients* 9:E866
3. Riahi, RR *et al.* [2016] Topical Retinoids: Therapeutic Mechanisms in the Treatment of Photodamaged Skin. *Am J Clin Dermatol* 17:265-276.
4. Kobayashi, D *et al.* [2011] The Effect of Pantothenic Acid Deficiency on Keratinocyte Proliferation and the Synthesis of Keratinocyte Growth Factor and Collagen in Fibroblasts. *J Pharmacol Sci* 115:230-234.
5. Wohlrab, J & Kreft, D [2014] Niacinamide – Mechanisms of Action and Its Topical Use in Dermatology. *Skin Pharmacol Physiol* 27:311-315.
6. Gehring, W [2004] Nicotinic Acid/Niacinamide and the Skin. *J Cosmet Dermatol* 3:88-93.
7. Cosmetic Ingredient Review [2005] Final Report of the Safety Assessment of Niacinamide and Niacin. *Int J Toxicol* 24:1-31.
8. Matts, PJ *et al.* [2002] A Review of the Range of Effects of Niacinamide in Human Skin. *IFSCC Magazine* 5:285-289.
9. Mi, T. *et al.* [2018]. Niacinamide and 12-hydroxystearic acid prevented benzo[a]pyrene and squalene peroxides induced hyperpigmentation in skin equivalent. *Exp Dermatol* 28:742-746.
10. Hakozaki, T *et al.* [2002] The Effect of Niacinamide on Reducing Cutaneous Pigmentation and Suppression of Melanosome Transfer. *Brit J Dermatol* 147:20-31.
11. Greatens, A *et al.* [2005] Effective Inhibition of Melanosome Transfer to Keratinocytes by Lectins and Niacinamide Is Reversible. *Exp Dermatol* 14:498-508.
12. Ando, H *et al.* [2012] Melanosomes Are Transferred from Melanocytes to Keratinocytes through the Processes of Packaging, Release, Uptake, and Dispersion. *J Invest Dermatol* 132:1222–1229.
13. Lo, JA & Fisher, DE [2014] The Melanoma Revolution: From UV Carcinogenesis to a New Era in Therapeutics. *Science* 346:945-949.
14. Cui, R *et al.* [2007] Central Role of p53 in the Suntan Response and Pathologic Hyperpigmentation. *Cell* 128:853-864.
15. Navarrete-Solis, J *et al.* [2011] A Double-Blind, Randomized Clinical Trial of Niacinamide 4% versus Hydroquinone 4% in the Treatment of Melasma. *Dermatol Res Pract* 2011: 379173.
16. Bissett, DL *et al.* [2003] Topical Niacinamide Provides Skin Aging Appearance Benefits while Enhancing Barrier Function. *J Clin Dermatol* 32S:9-18.
17. Tanno, O *et al.* [2000] Nicotinamide increases biosynthesis of ceramides as well as other stratum corneum lipids to improve the epidermal permeability barrier. *Br J Dermatol* 143:524-531.
18. Mohammed, D *et al.* [2013] Influence of Niacinamide Containing Formulations on the Molecular and Biophysical Properties of the Stratum Corneum. *Int J Pharmaceutics* 441:192-201.
19. Saxena, R *et al.* [2018] Comparison of Healthy and Dandruff Scalp Microbiome Reveals the Role of Commensals in Scalp Health. *Front Cell Infect Microbiol* 8:346.
20. Contassot, E & French, LE [2014] New Insights into Acne Pathogenesis: Propionibacterium Acnes Activates the Inflammasome. *J Invest Dermatol* 134:310-313.
21. Williams, MR & Gallo, RL [2017] Evidence that Human Skin Microbiome Dysbiosis Promotes Atopic Dermatitis. *J Invest Dermatol* 137:2460-2461.
22. Troccaz, M *et al.* [2015] Mapping Axillary Microbiota Responsible For body odours using a culture-independent approach. *Microbiome* 3:3.
23. James, AG *et al.* [2013] Microbiological and Biochemical Origins of Human Axillary Odour. *FEMS Microbiol Ecol* 83:527–540.
24. Krutmann, J [2009] Pre- and probiotics for human skin. *J Dermatol Sci* 54:1-5.
25. Mathapathi, MS *et al.* [2017] Niacinamide Leave-on Formulation Provides Long-lasting Protection Against Bacteria *In Vivo*. *Exp Dermatol* 26:827-829.
26. Shalita, AR *et al.* [1995] Topical nicotinamide compared with clindamycin gel in the treatment of inflammatory acne vulgaris. *Int J Dermatol* 34:434-7.
27. Khodaeiani, E *et al.* [2013] Topical 4% Nicotinamide vs. 1% Clindamycin in Moderate Inflammatory Acne Vulgaris. *Int J Dermatol* 52:999-1004.
28. Draelos, ZD *et al.* [2006] The Effect of 2% Niacinamide on Facial Sebum Production. *J Cosmet Laser Ther* 8:96-100.
29. Schwartz, J *et al.* [2014] Scalp Care Efficacy of a Leave-on Treatment Based on Niacinamide, Caffeine, and Panthenol. *J Am Acad Dermatol* 70:AB54.



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