



Niacinamide Beyond Skincare: Emerging Uses And Benefits

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Abstract:

Niacinamide a form of Vit B3, is widely recognized for its dermatological benefits; however, emerging research suggests its therapeutic potential extends far beyond skincare. Its anti-inflammatory properties make it beneficial for managing conditions like acne, rosacea, psoriasis, eczema, dermatitis, etc. Its role in cellular metabolism suggest implication for metabolic disorders and its management. Niacinamide shows improved insulin sensitivity and reduced oxidative stress, which is beneficial in diabetes management and it has potential to enhance immune function and support chemotherapy, positioning it as a valuable ally in cancer treatment. Moreover, its neuroprotective properties are gaining attention in the contest of neurodegenerative diseases like Alzheimer's and Parkinsons, where niacinamide may support cognitive functions and neuronal integrity. Niacinamide has a range of uses across various industries including pharmaceuticals, food industry, cosmetics, agriculture, biotechnology, nutraceuticals, textiles, cleaning products, bio polymer, beverages etc.

This review emerges niacinamide as a multifaceted compound with significant potentials other than skin care. It is essential to fully understand its mechanisms and broaden its usage across industries. By leveraging its diverse properties, niacinamide may contribute substantially to health and wellness initiatives in various contexts.

Index Terms - anti-inflammatory, cellular metabolism, insulin sensitivity, skincare.

1.Introduction

Niacinamide, also known as vitamin B3, is an essential nutrient that the body converts into the co-factors NADH and NADPH, which are crucial for various biochemical processes. A deficiency in this water-soluble vitamin can lead to pellagra, a condition characterised by symptoms such as dermatitis and red lesions. Three main forms of vitamin B3 are commonly used in topical skincare products: niacinamide (also known as nicotinamide), nicotinic acid, and nicotinate esters (such as benzyl nicotinate and myristoyl nicotinate)[**Error! Reference source not found.**].

Nicotinic acid is a white crystalline solid that remains stable in air at room temperature. It is moderately soluble in water and alcohol, but insoluble in ether. An aqueous solution of nicotinic acid shows maximum ultraviolet absorbance at 263 nm [**Error! Reference source not found.**].

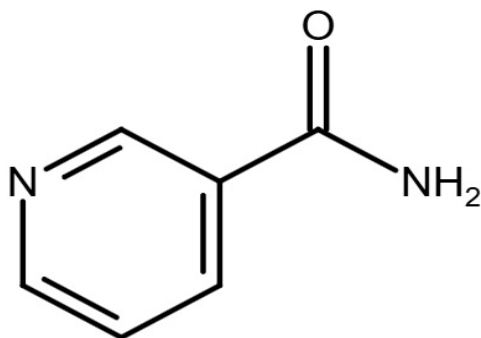
1.1. Basic Properties

Niacinamide plays a crucial role in certain coenzymes, including niacinamide adenine dinucleotide (NAD⁺) and its reduced form (NADH), as well as niacinamide adenine dinucleotide phosphate (NADP⁺) and its reduced form (NADPH) [3]. In the human body, niacinamide functions similarly to nicotinic acid, but it has distinct pharmacological effects and side effects [**Error! Reference source not found.**].

1.2. Plant Resources

Niacinamide is found in plant resources like fruits (bananas, apples), vegetables (mushrooms, carrots, and tomatoes), nuts(roasted peanuts, sunflower seeds, and almonds), legumes (soya beans, lentils). It is also obtained from meat (chicken, beef), seafood (tuna, salmon) [**Error! Reference source not found.**].

1.3. Chemical structure



2.Mechanism of action

Since niacinamide is essentially involved in the cellular energy metabolism, the regulation of DNA synthesis, as well as in transcription processes, various biological effects can be observed after in vitro and in vivo substitution. These effects are particularly striking in quantities that exceed physiological concentration, as they can be reached by epicutaneous application of niacinamide containing galenic systems. There are indications that these effects can be relevant for dermatological practice [**Error! Reference source not found.**]. Nicotinamide is consumed through food as part of pyridine nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP) found in plant and animal tissues. Once these coenzymes are broken down, nicotinamide is nearly fully absorbed in the small intestine. After absorption, it is stored as NAD in the liver, and excretion occurs through the kidneys. Additionally, tryptophan is converted into nicotinamide via the kynurenine-anthranilate pathway in the liver, allowing tryptophan to meet the body's need for dietary nicotinic acid [**Error! Reference source not found.**].

2.1.Absorption

Both nicotinamide and nicotinic acid can be absorbed through the stomach lining, but absorption is faster in the small intestine. For intact nucleotides, pyrophosphatase activity in the upper small intestine breaks down NAD(P) to produce NMN, which is then rapidly hydrolyzed into nicotinamide riboside and eventually free nicotinamide. At low concentrations, both nicotinic acid and nicotinamide are absorbed via sodium-dependent facilitated diffusion or carrier-mediated transport, utilizing proton cotransporters and anion antiporters. At higher concentrations, both forms are absorbed through passive diffusion. Once inside the enterocyte, nicotinamide can be converted to NAD or released into the portal circulation. While some nicotinic acid enters the blood in its original form, most of it is converted to NAD in the enterocyte via the Preiss–Handler pathway. As needed, NAD glycohydrolases in the enterocytes release nicotinamide into the plasma, which serves as the primary circulating form of niacin [Error! Reference source not found.].

2.2.Distribution and metabolism

Niacin compounds entering the portal circulation are either absorbed by erythrocytes or transported to the liver. Erythrocytes uptake nicotinic acid and nicotinamide through facilitated diffusion, converting them to nucleotides to maintain a concentration gradient. The liver, as a central processing organ for niacin, receives both nicotinamide and some nicotinic acid, and also releases nicotinamide from other tissues. In the liver, these compounds are metabolized to NAD or converted to substances for urinary excretion based on the body's niacin levels. The liver has a limited capacity to store NAD, and dietary nicotinamide can significantly increase liver NAD concentrations. NAD glycohydrolases in the liver may convert NAD into nicotinamide, which is then released to replenish other tissues. The liver also prepares niacin for excretion by producing methylation and hydroxylation products. In humans, nicotinamide is mainly methylated into N1-methylnicotinamide, while nicotinic acid is conjugated with glycine to form nicotinuric acid. High niacin intake can increase levels of these untransformed vitamers in urine and may also affect methyl donor status and blood homocysteine levels [Error! Reference source not found.].

3. Uses of niacinamide

3.1. Skincare

This vitamin is crucial for NAD⁺ synthesis, which plays a key role in redox reactions and energy production in skin cells. Additionally, niacinamide affects DNA repair and helps regulate cellular stress responses through various biochemical pathways [Error! Reference source not found.].

3.1. Antioxidants

Ingesting nicotinamide helps prevent lipid peroxidation and restores the levels of reduced antioxidants and antioxidant enzymes [Error! Reference source not found.].

3.2. Reduce wrinkles and fine lines

In a clinical trial, a moisturizing regimen with niacinamide, peptide pal-KTTKS, and retinyl propionate (RP) was compared to a prescription 0.02% tretinoin treatment. Both regimens significantly improved fine lines and wrinkles by 24 weeks, but the N/peptide/RP regimen was more effective earlier (after 8 weeks) and better tolerated, with fewer issues related to skin barrier function, redness, and dryness [Error! Reference source not found.].

3.3. Lightening effect

Niacinamide reversibly blocks the transfer of melanosomes from melanocytes to keratinocytes by inhibiting keratinocyte factors. This mechanism sets niacinamide apart from other skin lightening agents, such as arbutin and kojic acid, which directly inhibit tyrosinase [Error! Reference source not found.].

3.4. Anti acne treatment

Niacinamide is a recently approved anti-acne treatment with strong anti-inflammatory properties, which play a key role in its effectiveness. Recent studies have shown that topical niacinamide is highly tolerated by facial skin and offers additional benefits, such as reducing sebum production [Error! Reference source not found.].

4. Emerging medicinal uses

4.1. Lipid lowering

Niacin is an effective and unique lipid-regulating agent that lowers total plasma cholesterol, apolipoprotein B, triglycerides, very low-density lipoprotein (VLDL), and low-density lipoprotein (LDL) while increasing high-density lipoprotein (HDL) levels. It also reduces small, dense LDL particles and lipoprotein(a), while selectively raising LPA-I particles [Error! Reference source not found.].

4.2. Blood pressure management

The strong acute blood pressure-lowering effects of niacin infusion in hypertensive patients may be due to a reduced ability to adjust large-artery compliance. Individuals with hypertension often have decreased vascular compliance and increased vascular stiffness, making their blood vessels less responsive to changes in vasoconstrictor hormones [Error! Reference source not found.].

4.3. Alzheimer's disease

Nicotinamide protects neuronal and vascular cells from various forms of damage, including oxidative stress, anoxia, and toxins like homocysteine and amyloid-beta. It is a potential therapeutic agent for Alzheimer's disease, with studies suggesting it may improve cognitive function [Error! Reference source not found.].

4.4. Parkinsons disease

The levels of nicotinamide adenine dinucleotide (NAD) are reduced in Parkinson's disease (PD), and this decrease has been linked to various age-related neurodegenerative conditions [Error! Reference source not found.]. Nicotinamide (NAM), a biologically active form of vitamin B3, serves as a precursor to the cofactor nicotinamide adenine dinucleotide (NAD), which is crucial for energy metabolism and other essential cellular functions. NAM has shown numerous beneficial effects and is used in the treatment of various conditions [Error! Reference source not found.].

4.5. Cancer treatment

Chemoprevention- Niacinamide has been shown to have chemopreventive properties, reducing the risk of certain types of cancer, such as skin and colon cancer. In various animal and human studies, both topical and oral use of niacin and its derivative, nicotinamide (niacinamide), have been shown to reduce UV-induced immunosuppression, a factor believed to contribute to the risk of skin cancer [Error! Reference source not found.].

4.6. Radio sensitization

Niacinamide has been found to enhance the effectiveness of radiation therapy in cancer treatment. Radiosensitization by nicotinamide and related compounds has been extensively documented both in vitro and in vivo across various tumor systems. In vitro studies suggest that their effect is due to the inhibition of the repair of radiation-induced potentially lethal damage (PLD) [Error! Reference source not found.].

4.7. Diabetes Management

Niacin is a key treatment for patients with type 2 diabetes (T2DM) because of its wide-ranging effects on lipid regulation [**Error! Reference source not found.**]. Niacin increased both HDL-C and HDL2-C levels while lowering the total cholesterol to HDL-C ratio. The study shows that niacin raised glucose, insulin, and C-peptide levels in nondiabetic, postmenopausal women [**Error! Reference source not found.**].

4.8. Arthritis treatment

It has been effectively used to treat acute schizophrenia, and they can still be beneficial when combined with electroconvulsive therapy (ECT) in well-established cases. However, they are not very effective for chronic patients in mental hospitals. Additionally, nicotinic acid is the most effective, affordable, and safe substance for lowering cholesterol, with minimal impact on dietary habits and no significant side effects [**Error! Reference source not found.**]. It improved arthritis symptoms, reduced the need for anti-inflammatory drugs, and increased joint mobility [**Error! Reference source not found.**].

4.9. Atherosclerosis

The direct effect of niacin in enhancing the redox potential of aortic endothelial cells, along with its vascular anti-inflammatory properties, may help explain its proven benefits in atherosclerotic cardiovascular disease [**Error! Reference source not found.**].

4.10. Pellegra

Pellagra is a disease caused by a lack of niacin (vitamin B3) in the diet. It is characterized by the "four Ds" including dermatitis, diarrhea, dementia and death. Although this disease has become rare in developed countries, it remains prevalent in underdeveloped nations. Pellagra is commonly found in individuals whose diet is mainly composed of maize, as well as in malnourished individuals and alcoholic men. Additional risk factors for vitamin B3 deficiency include anorexia nervosa, AIDS, cancer, chemotherapy and malabsorptive disorders like Crohn's disease. Niacin is often used to treat pellagra because it is more stable and less likely to cause skin flushing than niacin [**Error! Reference source not found.**].

5. Clinical Evidence

Recent clinical trials

The trial was a randomized controlled study conducted on 25 healthy Caucasian participants. The serum was applied once daily to the designated area, and skin parameters were measured using a non-invasive bioengineering method. Niacinamide is known for promoting keratinocyte differentiation and preventing their senescence due to oxidative stress, making it an effective ingredient for strengthening the skin barrier. It has been extensively researched in dermatology for its benefits in treating conditions like acne vulgaris and psoriasis, as well as its potential in skin cancer prevention. Additionally, niacinamide is widely used in cosmetics for its anti-inflammatory properties, ability to reduce skin pigmentation, anti-aging effects, and its role in enhancing intercellular lipid production, which helps improve the barrier function of the stratum corneum [**Error! Reference source not found.**]. A relatively recent finding is the ability of niacinamide to impact UV-induced changes in skin. For example, in vitro testing showed that niacinamide can reduce production of PGE2 from keratinocytes when stressed with non-lethal fluencies of UVB. Observations of cellular morphology also suggest an ability to protect overall integrity of the cellular structure from UV-induced changes in vitro. This supports published data showing the ability of both topical and oral niacinamide to prevent UV-induced immunosuppression [**Error! Reference source not found.**].

6. Common side effects

6.1. Skin flushing

Some research suggests that the release of prostaglandin D2 (PGD2) from dermal macrophages may play a role in causing the cutaneous flushing associated with niacin use [Error! Reference source not found.]. A common side effect of nicotinic acid doses over 75 mg is a tingling or flushing sensation in the skin, which occurs due to the dilation of blood vessels. This effect is part of nicotinic acid's natural action and is also why it is used for certain therapeutic purposes [Error! Reference source not found.].

6.2. Blurred vision

Less common side effects of niacin include blurred vision, which can result from cystoid macular edema, as well as nausea and vomiting. Additionally, niacin may worsen existing peptic ulcers in some individuals [Error! Reference source not found.].

6.3. Elevation of liver enzymes

A potential side effect of high-dose niacin therapy is an increase in liver enzyme levels, which is often cited by doctors as a major concern. However, this concern may be overstated. According to William B. Parsons Jr. from the Mayo Clinic, a slight to moderate elevation in liver enzymes simply reflects increased liver activity, not liver damage. This is because niacin is a precursor for NAD, a crucial cofactor involved in numerous biochemical reactions throughout the body, particularly in the liver [Error! Reference source not found.].

6.4. Gastrointestinal upset

It was reported that niacin can sometimes cause nausea and vomiting, and this reaction is more common with higher doses. The threshold for this side effect varies among individuals, with symptoms potentially occurring at doses ranging from 3 grams to as much as 30 grams per day [Error! Reference source not found.].

7. Conclusion

This review highlights the versatile uses of niacinamide in cosmetic formulations, focusing on its ability to improve skin health and appearance. Beyond basic moisturization, niacinamide offers benefits for conditions like rosacea by strengthening the skin barrier. It's a valuable and cost-effective ingredient for dermatologists, offering skin-friendly solutions for various dermatological issues. In selecting ingredients for cosmetic products, clinical proof is just as essential as in vitro studies. Effective clinical studies should be well-designed, including elements like statistical power, double-blind controls, randomization and objective measures. These clinical efforts ensure that niacinamide's benefits are backed by solid evidence, making it a reliable ingredient for improving skin appearance in a real-world, patient-relevant manner. The emerging uses of niacinamide, particularly in dermatology, go beyond skincare, offering significant benefits for skin disorders and improving overall skin health [Error! Reference source not found.]. Niacinamide's effect on controlling skin aging and pigmentation could be attributed to its own unique properties, the effects of other metabolites it produces, or possibly a combination of both [Error! Reference source not found.].

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