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Exploring the Role of NAD^+ in Cellular Metabolism, Aging, and Skin Rejuvenation: A Cosmetological Perspective

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Abstract: ***Nicotinamide Adenine Dinucleotide (NAD^+) is an essential coenzyme required for DNA repair, energy synthesis, and cellular metabolism. Its essential function in skin health, age modulation, and rejuvenation therapies has been demonstrated by recent developments in dermatological and cosmetological sciences. Age and environmental stress cause NAD^+ levels to gradually drop, which results in decreased collagen synthesis, diminished mitochondrial function, and noticeable skin aging (Verdin, 2015). The biochemical relevance of NAD^+, its molecular pathways affecting skin physiology, and its new uses in cosmetic and regenerative cosmetology are all examined in this research. The study emphasizes the significant role of NAD^+ restoration techniques-such as topical NAD^+ formulations, nicotinamide riboside (NR), and nicotinamide mononucleotide (NMN) supplementation-in boosting skin healing, firmness, and brightness through an in-depth scientific analysis. The results substantiate the implementation of NAD^+-enhancing treatments as a potential development in contemporary cosmetic procedures. Nicotinamide Adenine Dinucleotide (NAD^+) is a key chemical in aging biology and aesthetic dermatology as it is an essential coenzyme involved in mitochondrial energy production, cellular repair, and genomic integrity. Skin aging and cellular senescence are accelerated by age-related declines in NAD^+, which also contribute to diminished sirtuin activity, poor oxidative metabolism, and hampered DNA repair (Verdin, 2015). According to research, NAD^+ depletion reduces fibroblast activity and extracellular matrix integrity, which are important causes of wrinkles, laxity, and pigmentation. It also increases oxidative stress and alters mitochondrial function (Poljsak & Milisav, 2016). Nicotinamide riboside (NR) and nicotinamide mononucleotide (NMN) supplements increase cellular NAD^+ pools, which improve skin resilience, restore metabolic efficiency, and encourage collagen formation (Rajman et al., 2018; Yoshino et al., 2018). Niacin derivatives' involvement in skin barrier repair, inflammatory control, and photoprotection is further highlighted by dermatological and nutritional research, which support their incorporation into cosmetology (Bogan & Brenner, 2008). According to recent research, NAD^+ is particularly potential for skin renewal, repair responses, and recovery after aesthetic procedure (Knutson et al., 2020). With everything considered, NAD^+ restoration offers therapeutic potential for anti-aging, regenerative skin care, and increased cellular vitality, making it a scientifically supported approach in contemporary cosmetology.***

Keywords: NAD^+, Skin Aging, Cosmetology, DNA Repair, Mitochondrial Health, Nicotinamide Riboside, Anti-Aging

1. Introduction

Nicotinamide Adenine Dinucleotide (NAD^+) is a metabolic coenzyme found within all living cells. It is essential for cellular vitality, metabolic efficiency, and genomic stability. It takes part in vital metabolic processes, mainly serving as an electron carrier that promotes redox reactions in pathways that generate energy. NAD^+ promotes ATP production and maintains cellular homeostasis through its participation in glycolysis, the TCA cycle, and oxidative phosphorylation (Verdin, 2015).

As a substrate for sirtuins and PARP enzymes, which are essential proteins involved in DNA repair, chromatin remodeling, cellular stress response, and longevity control, NAD^+ plays an important regulatory role beyond energy metabolism (Rajman et al., 2018; Poljsak & Milisav, 2016). These NAD-dependent enzymes ensure balanced gene expression, safeguard genomic DNA, and preserve mitochondrial integrity-all of which are essential for healthy cellular function.

due to its impact on skin health, aging, and restoration, NAD^+ has drawn a lot of attention in the fields of cosmetology and skin science. Age-related declines in NAD^+ levels result in decreased mitochondrial efficiency, elevated oxidative stress, diminished fibroblast activity, and weakening of the extracellular matrix, all of which contribute to early skin aging, pigmentation, and elasticity loss (Verdin, 2015; Knutson et al., 2020).

Dietary precursors including nicotinamide, nicotinamide riboside (NR), and nicotinamide mononucleotide (NMN) can replenish NAD^+ pools by entering the salvage pathway and restoring intracellular NAD^+ levels (Bogan & Brenner, 2008; Yoshino et al., 2018).Research shows these precursors enhance metabolic resilience, boost DNA repair, and promote dermal regeneration, making NAD^+ restoration a promising strategy in modern cosmetology and anti-aging treatments (Knutson et al., 2020).

Aim of the Study

To evaluate the role of NAD^+ in cellular metabolism and its potential applications in cosmetology for enhancing skin health, delaying aging, and promoting rejuvenation.

Objectives

- To review the biochemical structure and metabolic functions of NAD^+.
- To analyze the correlation between NAD^+ depletion and visible signs of skin aging.
- To explore the therapeutic potential of NAD^+ precursors in aesthetic and regenerative skin treatments.
- To assess current and future applications of NAD^+-based formulations in cosmetology practice.

Biochemical Overview of NAD^+

Nicotinamide Adenine Dinucleotide (NAD^+) is an essential dinucleotide coenzyme made up of nicotinamide and adenine

joined by phosphate groups. NAD^+ exists in two interconvertible forms: oxidized NAD^+ and reduced NADH, making it a key electron carrier in metabolic processes. It is essential for oxidative phosphorylation, glycolysis, and the tricarboxylic acid cycle, which facilitates effective ATP synthesis (Verdin, 2015).

Beyond its metabolic function, NAD^+ is an essential substrate for PARP and sirtuins, which modulate inflammation, DNA repair, chromatin remodeling, and cellular stress reactions (Rajman et al., 2018; Poljsak & Milisav, 2016). These mechanisms preserve genomic stability and mitochondrial function, both of which are necessary for young cellular activity.

Because to increasing PARP consumption, chronic inflammation, and mitochondrial malfunction, NAD^+ levels normally decrease with age, impairing energy metabolism and hastening aging (Yoshino et al., 2018). To replenish NAD^+ levels, cells use dietary precursors including nicotinamide, nicotinamide riboside (NR), and nicotinamide mononucleotide (NMN), which improve metabolic resilience and cellular repair processes (Bogan & Brenner, 2008). In skin biology, appropriate NAD^+ availability supports collagen synthesis, antioxidant defense, and dermal regeneration (Knutson et al., 2020).

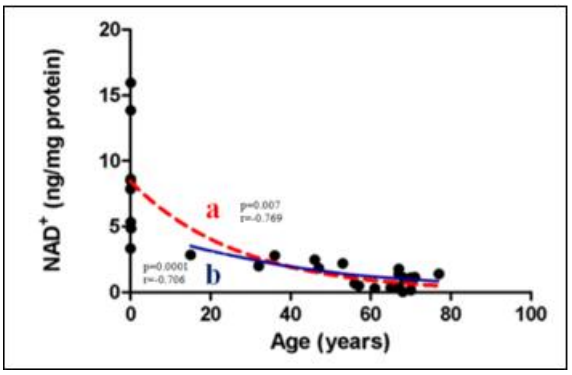
NAD^+ and the Biology of Aging

Aging is driven by progressive declines in **mitochondrial function**, **DNA repair capacity**, and **cellular stress resistance**-all of which are tightly regulated by NAD^+. Research shows that **NAD^+ levels drop by nearly 50% every 20 years**, primarily due to increased consumption by PARPs (activated during DNA damage), chronic inflammation, and mitochondrial dysfunction (Verdin, 2015).

Low NAD^+ levels affect the action of sirtuins, a family of NAD^+-dependent enzymes that govern longevity pathways such mitochondrial biogenesis, oxidative stress response, and metabolic stability (Rajman et al., 2018). Lower sirtuin activity causes cellular senescence, collagen loss, poor energy metabolism, and apparent skin aging.

Similarly, declining NAD^+ impairs PARP-mediated DNA repair, which permits the development of mutations, genomic instability, and persistent inflammation-all of which are major signs of aging (Poljsak & Milisav, 2016). Further research demonstrates that NAD^+ restoration via precursors like NR and NMN improves cellular regeneration, lowers oxidative stress, and increases mitochondrial activity (Yoshino et al., 2018; Bogan & Brenner, 2008).

NAD^+ replenishment promotes fibroblast activity, collagen production, and barrier repair in skin biology, while NAD^+ depletion causes loss of elasticity, delayed wound healing, and increased UV exposure (Knutson et al., 2020).



Cellular Energy and Skin Function

NAD^+ is essential for maintaining the high energy demands of skin cells, particularly **keratinocytes** in the epidermis and **fibroblasts** in the dermis. These cells rely on continuous ATP production for barrier maintenance, collagen synthesis, and repair processes. NAD^+ drives ATP generation by participating in **glycolysis**, the **TCA cycle**, and **oxidative phosphorylation**, ensuring optimal mitochondrial output (Verdin, 2015).

Healthy mitochondrial function is supported by adequate NAD^+ levels, which enable fibroblasts to create collagen and extracellular matrix components that are essential for the firmness and elasticity of skin. Reduced mitochondrial efficiency due to declining NAD^+ results in reduced barrier function, slower wound healing, and more oxidative damage (Rajman et al., 2018).

Sirtuins, which improve cellular survival, control energy balance, and shield skin cells from UV-induced stress and inflammation, are likewise activated by NAD^+ (Poljsak & Milisav, 2016). Fibroblast activity, dermal regeneration, and youthful skin physiology are all improved by supplementing NAD precursors such NMN and NR (Yoshino et al., 2018; Knutson et al., 2020).

Protection Against UV and Oxidative Stress

NAD^+ plays a central protective role against UV-induced cellular damage and oxidative stress by supporting **DNA repair**, **mitochondrial stability**, and **antioxidant defense systems**. UV radiation causes DNA strand breaks that activate **PARP enzymes**, which consume NAD^+ to repair damage and maintain genomic integrity; adequate NAD^+ is therefore essential for efficient photodamage recovery (Verdin, 2015; Rajman et al., 2018).

Additionally, NAD^+ stimulates sirtuins, especially SIRT1, which improves resistance to oxidative stress by controlling the expression of antioxidant genes, inflammatory pathways, and mitochondrial function (Poljsak & Milisav, 2016). Increased ROS buildup, photoaging, uneven pigmentation, and collagen breakdown are all consequences of reduced NAD^+ levels impairing these processes.

Supplementing with NAD^+ precursors such NMN and NR increases intracellular NAD^+ pools, boosting DNA repair capability and cellular tolerance to UV exposure (Yoshino et al., 2018). In skin biology, this leads to enhanced dermal

structural integrity, less oxidative damage, and increased fibroblast function (Knutson et al., 2020).

Collagen and Elasticity Restoration

NAD^+ plays a crucial role in maintaining and restoring **collagen integrity**, **skin elasticity**, and overall dermal structure. Fibroblasts- the primary cells responsible for collagen and extracellular matrix (ECM) production-require high NAD^+ levels to support mitochondrial energy generation, protein synthesis, and cellular repair (Verdin, 2015). As NAD^+ declines with age, fibroblast activity decreases, leading to reduced collagen formation, fragmentation of existing collagen fibers, and visible skin aging.

NAD^+ stimulates sirtuins, particularly SIRT1, which improves fibroblast survival, controls extracellular matrix remodeling, and prevents collagen-degrading enzymes such matrix metalloproteinases (MMPs). Stronger dermal architecture and increased flexibility are supported by this (Rajman et al., 2018; Poljsak & Milisav, 2016).

Furthermore, collagen is shielded against UV-induced deterioration and glycation-related stiffness, two significant causes of skin aging, by decreased oxidative stress brought on by increased NAD^+ levels.

Intracellular NAD^+ pools are restored by supplementing NAD^+ precursors such NMN and NR, which encourages fibroblasts to produce new collagen and gradually improves skin firmness and wrinkle depth (Yoshino et al., 2018; Knutson et al., 2020). Because of these metabolic effects, NAD^+ is a useful target in regenerative dermatology and anti-aging cosmetology.

Restoring NAD^+ Levels

In order to improve skin health, mitochondrial function, and reverse molecular aging, NAD^+ levels must be restored. Due to decreased production routes, persistent inflammation, and increasing consumption by PARPs, NAD^+ naturally decreases with age (Verdin, 2015). Restoring precursors and improving cellular recycling processes are the main goals of restoration techniques.

NAD precursors: Cells use the salvage pathway to produce NAD precursors, mainly by using: Nicotinamide (NAM), Nicotinamide Riboside (NR), Nicotinamide Mononucleotide (NMN).

These precursors effectively transform into NAD^+, which enhances tissue repair, lowers inflammation, and improves mitochondrial function (Bogan & Brenner, 2008; Yoshino et al., 2018).

Activation of Sirtuins and DNA Repair: Increased NAD^+ supports sirtuin activity and PARP-mediated DNA repair, stabilizing the genome and improving cellular resilience (Rajman et al., 2018).

Reduction of NAD^+ Consumption: Lowering chronic inflammation and oxidative stress helps preserve NAD^+ by reducing overactivation of PARPs and CD38, an NAD^+-degrading enzyme (Poljsak & Milisav, 2016).

Topical and Aesthetic Applications: In cosmetology, NAD^+ restoration is achieved through:

- Topical NAD^+ or NMN serums
- Mesotherapy with NAD^+ blends
- Supportive antioxidant therapies to reduce oxidative depletion

These approaches improve collagen synthesis, hydration, and dermal regeneration (Knutson et al., 2020).

2. Conclusion

NAD^+ stands as a cornerstone molecule at the intersection of biochemistry and cosmetology. Its roles in energy metabolism, DNA repair, and antioxidant defense highlight its importance in maintaining skin vitality. NAD^+ supplementation- whether oral, topical, or procedural- offers a promising pathway for true cellular rejuvenation.

NAD^+ is a vital biomolecule that connects cellular metabolism to skin health, making it an important factor in modern cosmetology practices. Its critical function in mitochondrial energy production, DNA repair, redox balance, and sirtuin activity regulation emphasizes its significance in preserving youthful, robust skin. Fine lines, hyperpigmentation, dullness, and decreased suppleness are all signs of mitochondrial dysfunction, poor collagen synthesis, increased oxidative stress, and delayed cellular regeneration caused by age-related NAD^+ depletion. A scientific and comprehensive approach to rejuvenation is provided by restoring NAD^+ levels using topical preparations, oral precursors such NMN and NR, and supportive cosmetic therapies.

There is growing evidence that NAD^+ augmentation promotes the function of the epidermal barrier, increases fibroblast activity, improves skin hydration, and speeds up healing after surgery. Even if there are still issues with bioavailability and standardized procedures, ongoing developments in transdermal technology and nano-delivery systems are quite promising. NAD^+-based treatments are a revolutionary advancement as cosmetology moves toward molecular and regenerative techniques. Incorporating NAD^+ replenishment techniques into aesthetic care improves treatment results and promotes long-term skin health, making it a key component of upcoming anti-aging and skin-repair treatments.

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Author Profile

Dr. Bhakti Unecha is a qualified medical professional and faculty at I2CAN, Pune, with a strong academic and clinical background. She holds a Bachelor's degree in Homeopathic Medicine and Surgery (BHMS) and has further enhanced her expertise with a Post Graduate Diploma in Emergency Medical Services and a Post Graduate Diploma in Clinical Cosmetology. With over four years of clinical experience, Dr. Unecha actively practices as a consulting homeopath and cosmetologist. Her multimodal approach, combined with clinical experience and academic involvement, demonstrates her dedication to evidence-based treatment, patient-centered care, and the advancement of clinical cosmetology education.