



Exploring NAD+ in Aesthetics

Dr Nichola Conlon introduces how NAD+ brings cellular regenerative medicine into aesthetics

The field of aesthetic medicine is undergoing a pivotal change. The emergence of cellular regenerative therapies is providing practitioners with the chance to enhance their patients' health from the inside-out. By going beyond the surface and treating ageing at the cellular level, there is now the opportunity for true age reversal, helping patients to not only look younger, but also feel younger.

This shift in our approach to ageing owes to the fact that recent scientific advancements have shed light on the underlying cellular mechanisms driving the ageing process, and more importantly, how we can target these changes to restore cellular health. Restoration of the cellular molecule nicotinamide adenine dinucleotide (NAD+) has emerged as a frontrunner in restoring youthful cellular function by targeting the root causes of ageing.

What causes the ageing process?

Ageing is scientifically defined as the loss of the body's innate ability to repair and regenerate itself, allowing the accumulation of cellular damage.¹ This results in cellular dysfunction, causing the signs and symptoms of ageing. It is now widely accepted that all of the external manifestations that we associate with ageing such as frailty, fatigue and wrinkles, ultimately result from dysfunction at the cellular level.¹

While humans are living longer than ever before, a significant portion of later life is burdened with age-related diseases. By treating the ageing process itself, the goal is to extend healthspan – the portion of life lived in good health, free from frailty and disease.² Ageing is a biologically complex phenomenon, but research has now revealed the 12 key cellular changes that underpin the ageing process. These cellular changes are termed the 'Hallmarks of Ageing' (Figure 1).³ In the context of skin ageing, the histological changes that occur, such as a loss of collagen, elastin and a breakdown of the extracellular matrix (the scaffolding structure of the skin), are a result of the underlying cellular hallmarks of ageing.

These include genomic instability arising from failure to repair UV-induced DNA damage, reduced cell turnover due to mitochondrial dysfunction, degradation of the extracellular matrix due to chronic low-grade inflammation and decreased production of collagen and elastin as a result of senescent fibroblasts.⁴ The discovery of these hallmarks has fundamentally changed our view and approach to treating ageing, and current research is focused on finding treatments that target these hallmarks to restore youthful cellular function.

What is NAD+ and why is it linked to ageing?

NAD+ is a natural molecule found in every cell in the body, regulating more than 300 biological reactions. The most important of these reactions being cellular energy production, where it is critical for the production of the cellular energy molecule adenosine triphosphate (ATP) by the mitochondria, as well as its contribution to powering key maintenance and repair pathways which regulate cellular health.⁵⁻⁷ NAD+ has become an intense area of research among longevity scientists, as it has been found to play a key role in the cellular ageing process. Despite being critical for cellular function, research shows that NAD+ levels decline by approximately 50% every 20 years.⁸ Low NAD+ negatively impacts energy production, cell signalling and repair, resulting in an accumulation of damage and the negative health consequences associated with ageing.⁹ Studies show that age-dependent NAD+ decline is observed across all species and in several human tissues including the skin, liver, brain, skeletal muscle and immune

cells.⁷⁻¹⁰ NAD+ depletion is also observed in diseases associated with accelerated ageing, such as xeroderma pigmentosum group A and Cockayne Syndrome.¹¹

Benefits of NAD+ restoration

Restoration of age-depleted NAD+ has been found to positively impact all of the hallmarks of ageing, leading to a multitude of benefits. At the cellular level, NAD+ restoration improves mitochondrial function, enhances DNA damage repair, increases ATP production and activates proteins that are associated with healthy ageing called sirtuins (SIRT6).¹² At a whole-body level, boosting NAD+ has been demonstrated to restore age-associated muscle loss, increase endurance and strength, increase neurogenesis, enhance cognitive function and improve markers of metabolic health, all of which positively impact healthspan.⁷ NAD+ has also emerged as a potential therapeutic tool for several age-related diseases which are associated with NAD+ deficiency. These include metabolic disease, neurodegenerative disorders, liver disease, kidney diseases and cardiovascular diseases.^{13,14} The diverse protective and regenerative capacity of NAD+ is attributed to its involvement in restoring optimal function at the cellular level, by preventing and reversing the hallmarks of cellular ageing.

Methods to restore NAD+

In order to successfully restore cellular NAD+, there has been a lot of research into understanding the underlying cause of



Figure 1: The hallmarks of ageing.¹ Image adapted from Nuchido.

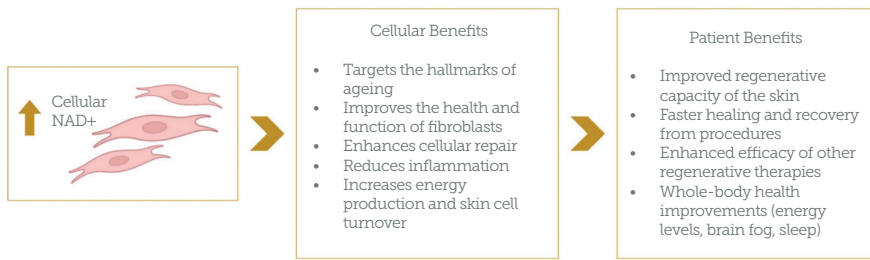


Figure 2: The role of NAD+ in aesthetics.^{4,7} Image adapted from Nuchido.

NAD+ decline with age. The latest scientific research demonstrates that NAD+ decline in older cells is ultimately a supply and demand issue. Older cells have more damage and inflammation which requires more NAD+ to fuel repair processes.¹⁵⁻¹⁷ At the same time, older cells lose their youthful ability to replenish NAD+ because the main enzyme that produces the majority of cellular NAD+ (named nicotinamide phosphoribosyl transferase) declines with age.^{18,19} Given the multitude of benefits associated with NAD+, several methods to restore NAD+ levels have emerged. The use of intravenous infusions of pure NAD+ and subcutaneous NAD+ injections have gained popularity; however, these methods should be approached with caution. This is because of the absence of clinical data surrounding the ability of the large and unstable NAD+ molecule to cross from the systemic circulation into cells where it performs its function.²⁰ Further studies are needed in this area to enhance understanding. Oral supplements consisting of NAD+ precursors (the raw materials used by the cell to produce NAD+) such as nicotinamide mononucleotide (NMN) have also become available. However, without restoring levels of nicotinamide phosphoribosyl transferase (NAMPT), the key NAD+ producing enzyme, supplying the cells with more precursor is akin to shipping raw material into a factory where all the machines are broken and expecting to see an increase in production.²¹⁻²³ Therefore, second generation NAD+ boosting supplements were formulated to combat this limitation. They not only provide NAD+ precursors, but also active ingredients that increase levels of the NAD+ producing enzyme NAMPT to reactive natural cellular NAD+ production pathways.^{24,25}

NAD+ in aesthetic medicine

Whilst popular aesthetic procedures such as dermal fillers and botulinum toxin strive to make the appearance of the signs of ageing less noticeable, they do little

to influence the ageing process itself. In comparison, NAD+ restoration goes beyond masking the effects of ageing and addresses the ageing process at its root cause (Figure 2). By targeting the underlying cellular hallmarks of ageing such as reducing inflammation and enhancing repair, NAD+ improves the health and function of dermal fibroblasts, leading to increased collagen and elastin production which fundamentally improves the structure and regenerative capacity of the skin from within.⁴ As the world's population gets older, addressing ageing at the cellular level is also becoming increasingly important. Not only are more people looking for ways to combat the signs of ageing, but many aesthetic procedures rely on the healing and regenerative capacity of the skin which is known to decline with age, leading to poor treatment outcomes and increased recovery and downtime. This means improving cellular health and resilience with NAD+ is of increasing importance to ensure the underlying cells are in an optimal condition to recover from aesthetic treatments. Furthermore, the efficacy of many current aesthetic procedures that induce a degree of superficial damage and irritation to the skin, such as microneedling, laser technologies and chemical peels, rely upon the activation of cellular stress pathways to trigger the clearance of damaged cells and stimulate the production of collagen. Many of these cellular pathways directly require adequate NAD+ levels for optimal function, meaning NAD+ restoration before and after these treatments can help to ensure that cells are primed to respond appropriately to these procedures.^{4,26,27} NAD+ restoration should also be considered for use alongside other emerging regenerative aesthetic treatments such as polynucleotides, exosomes and platelet-rich plasma (PRP). These treatments all work by surrounding the cells with signalling factors to restore

youthful cellular communication, one of the hallmarks of ageing.²⁸⁻³⁰ Combining these regenerative treatments with NAD+ increases their benefit, as NAD+ targets other hallmarks to enhance the health of the cells in a cumulative manner.⁴ Finally, the effects of NAD+ are not limited to the skin, but are body-wide, leading to improvements in patients' overall health. NAD+ is particularly beneficial for anyone experiencing signs of ageing such as fatigue, loss of cognitive function (brain fog) and sleep disturbances, all of which are linked to age-related NAD+ decline.³¹⁻³³

A new era of ageing science

NAD+ is part of a new era of cellular regenerative treatments which harness the body's natural protection and repair mechanisms to restore youthful cellular function. The introduction of NAD+ restoration to aesthetic medicine allows practitioners to go beyond the surface, truly addressing the effects of ageing in their patients, and is a valuable addition to any clinic that is proactively seeking to offer the latest age-reversal therapies.

Disclosure: Dr Nichola Conlon is the chief executive officer and shareholder of Nuchido Ltd. and has filed patents on NAD+ boosting therapies.



Dr Nichola Conlon is a molecular biologist specialising in the study of cellular ageing. She is passionate about translating the latest science into products that slow biological ageing. After a career in drug development, she founded Nuchido Laboratories. Dr Conlon recently spoke at the inaugural Medical Longevity Summit at CCR, which will take place again on October 10-11, 2024.

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