Not slowing aging, but reversing function.

NAD+ Recovery, Inside the Cell

Héjeuna's approach to aging begins where function is restored.

Héjeuna's Philosophy

From ECM to ICM

Conventional skin boosters have focused on the ECM (Extracellular Matrix), an approach centered on managing structures outside the cell. This strategy addresses the visible "outcomes" of aging.
Héjeuna reframed the question:

"Why do cells and tissues remain alive, yet fail to function properly?"

Functional Aging

When aging is viewed as a matter of time, it is simply aging. When viewed as a matter of function, it becomes functional aging. Traditional anti-aging strategies have managed "outcomes" through protection, supplementation, and stimulation. Anti-functional aging, by contrast, identifies cellular functional decline as the essence of agingand targets the restoration of function rather than external appearance.

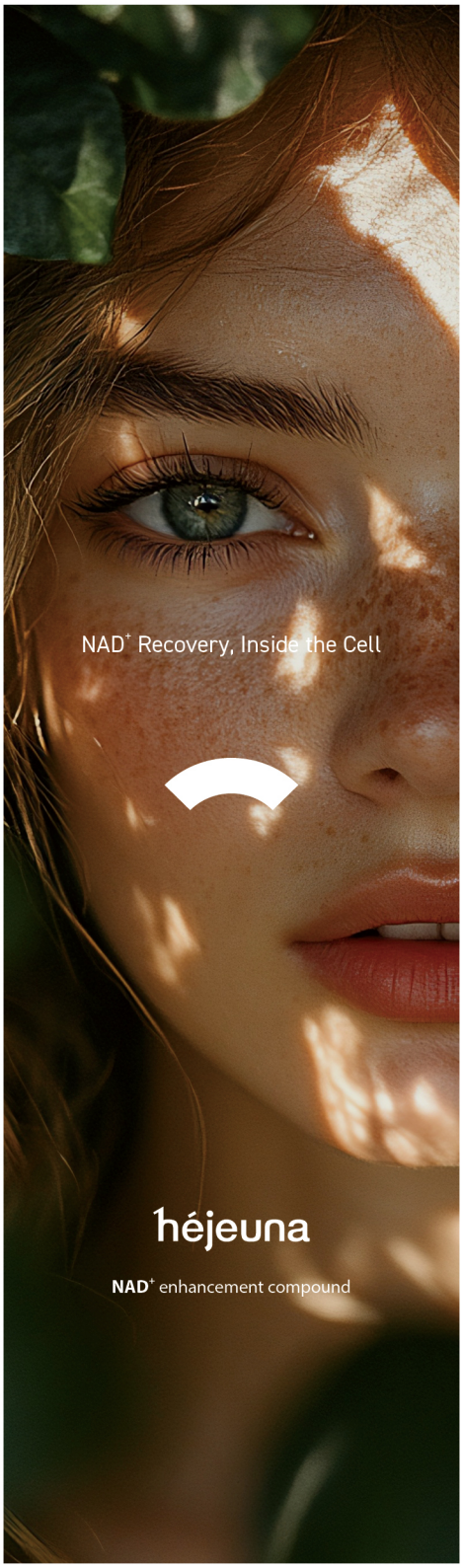
ICM, Intracellular Functional Molecule Restoring Intracellular Function

Héjeuna moves beyond the ECM.It directly restores the intracellular conditions required for function, namely cellular energy and redox balance,through an ICM (Intracellular Functional Molecule) approach. NAD+ recovery is not the goal itself,but the starting point that enables cells to function again.

ECM : Extracellular Matrix
ICM : Intracellular Functional Molecule

	Anti-aging (ECM Approach)	Functional Aging (ICM Approach)
Definition of Aging	Aging as the accumulation of time-dependent "outcomes"	Accumulation of cellular functional decline
Perspective on Aging	Aging, a problem of time	Functional aging, a problem of function
Primary Target	ECM, extracellular structures	ICM, intracellular functional state
Point of Intervention	Damage, defects, external changes	Cellular operating state, energy, redox balance
Approach	Management of outcomes	Restoration of causal conditions
Strategy	Supplementation, protection, stimulation	Functional recovery, condition restoration
Limitation	Slowing aging	Restoration, potential reversibility of aging
Core Molecules	Collagen, hyaluronic acid, etc.	NAD+, energy, redox balance
Conceptual Message	"Delay"	"Make it function again"

The essence of skin aging lies not in cellular aging itself, but in the progressive loss of cellular function



Key Changes Associated with Functional Aging of Skin Cells

Cause

1. Energy Depletion

- Mitochondrial dysfunction
- Reduced ATP production leads to slowed biosynthesis and repair processes

2. Redox Imbalance

- Decline in NAD+ levels and disruption of the NAD+/NADH balance
- Stagnant electron flow and accumulation of oxidative stress

3. Failure of Gene Regulation

- Inactivation of NAD+-dependent regulatory systems
- Impaired DNA repair and reduced stress response capacity

4. Disruption of ECM Production

- Decreased synthesis of collagen, elastin, and hyaluronic acid
- Degradation exceeds synthesis, resulting in structural breakdown

5. Attenuated Signaling Responsiveness

- Reduced responsiveness to regenerative and growth signals
- Persistent inflammatory signaling

6. Loss of Homeostasis

- Delayed recovery following damage
- Compromised barrier function and impaired healing capacity

Outcome

▼

ECM Decline (Structural Breakdown)

▼

Skin Aging

Wrinkles and loss of elasticity are not the cause, but the “outcomes.”
The solution to functional aging is not structural supplementation,
but restoring the conditions that allow cells to function again.

From ECM to ICM

Cellular function is restored not through structure, but through energy and redox balance

NAD+ Enhancement Compound COENZYME K

ECM-Oriented Approach (Conventional Skin Boosters)

Extracellular, outcome-focused

- ECM supplementation, stimulation, and protection
- External delivery of collagen and hyaluronic acid
- "Managing" structures that have already deteriorated
- Effects are temporary and consumptive

ICM-Oriented Approach

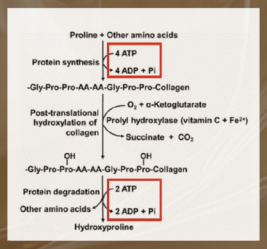
Intracellular, condition-restorative

- Restoration of intracellular energy and redox state
- Normalization of NAD+, ATP, and electron flow
- Restores the functional conditions that allow cells to resume synthesis and repair
- Structural recovery emerges as a downstream result

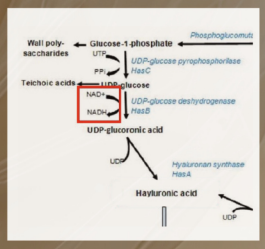
ECM is not a materials problem,but a matter of energy and redox state.

NAD+ and ATP are essential energy molecules required for the production of collagen and hyaluronic acid, which are critical for skin maintenance.

Ref.
Mouw, J. K., Ou, G., & Weaver, V. M. (2014).
Huang, W. Y., et al. (2019).



Collagen Biosynthesis



Hyaluronic Acid Biosynthesis

ECM does not function independently. Its synthesis, maintenance, and remodeling are entirely dependent on intracellular energy and redox state (ICM).

ECM-Specific Dependence on NAD+ and ATP

ECM Component	ATP Dependence	NAD+ Dependence	Notes
Collagen	★★★	★★	Synthesis and processing
Hyaluronic Acid	★★	★★★	Direct utilization of NAD+
Elastin	★★	★★	Maintenance and cross-linking
Proteoglycans	★★★	★★★	Highly sensitive to metabolic decline
GAGs	★★	★★★	Energy-demanding synthesis
Basement ECM	★★	★★	Secretion and assembly
ECM Remodeling	–	★★★	Functional maintenance

Why
did NAD+ become central to aging?

Because NAD+ is not just a molecule,
but a turning point in how we understand aging

NAD+ Is Not a New Molecule

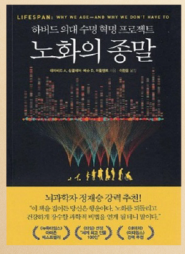
NAD+ has been studied for over a century and is a fundamental molecule that sustains energy metabolism and cellular survival.

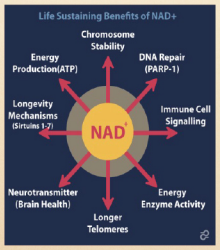
A Shift in the Aging Question Placed NAD+ at the Center

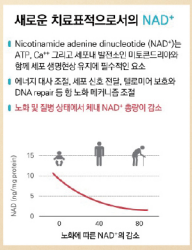
Aging is increasingly being redefined not as the passage of time, but as the cumulative decline of cellular function, where cells remain alive yet fail to operate properly.

NAD+ Is the Common Denominator of Cellular Function

NAD+ is the starting point for energy production, DNA repair, stress response, and signaling pathways. As NAD+ declines, structural components may remain, but cellular function comes to a halt.

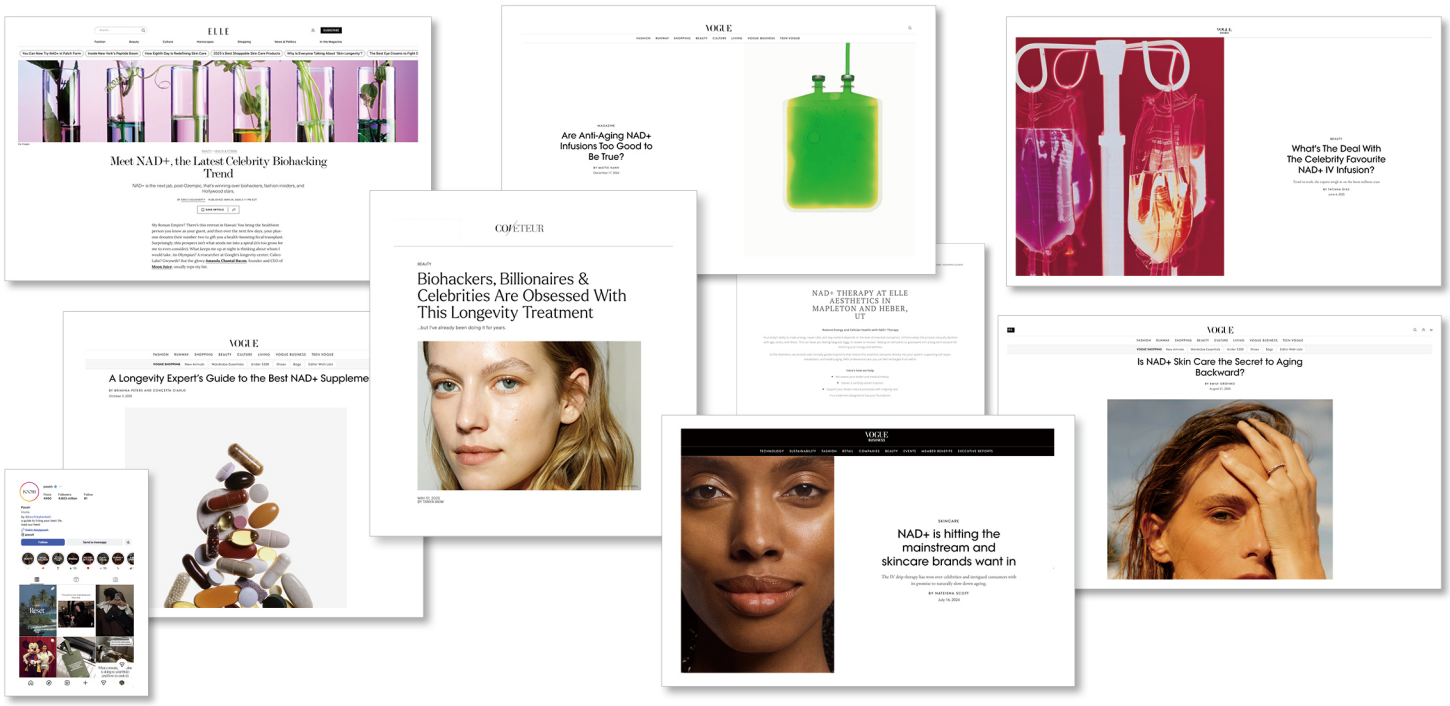






> **Aging is a disease that can be treated.Enhancing NAD+ is one of the key therapeutic strategies.**
>
> David A. Sinclair

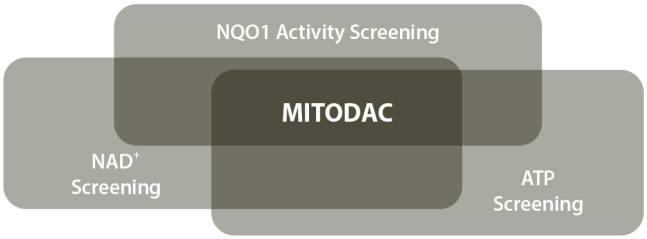
Maintaining NAD+ levels is an essential factor in anti-aging mechanisms, including improved mitochondrial function and energy production, as well as enhanced DNA repair and telomere protection.



Development capacity

MITODAC is an NQO1-targeted, Coenzyme K–based platform designed to regulate NAD+ and address skin aging

A proprietary dual-activation platform for NAD+ and ATP, MITODAC

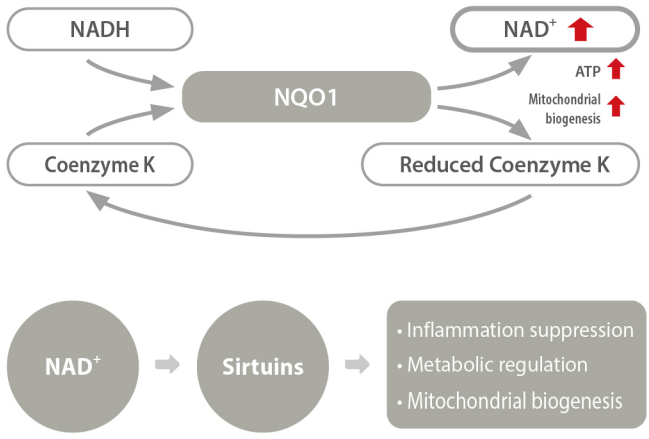


Development status of NQO1-targeted Coenzyme K

- Advanced development of NQO1-targeted Coenzyme K molecules
- Library of over 700 proprietary lead compounds
- Robust IP portfolio with over 40 foundational patents

Starting with the development of therapeutics for PSC, PBC, and LHON, we are advancing a broad drug development pipeline targeting diseases driven by NAD+ depletion and ATP deficiency.

NQO1-Activated NAD+ Redox Loop ON Technology



FDA IND approval for Phase 2 clinical trials **Coenzyme K designated as an Orphan Drug in Europe**	PSC (Primary Sclerosing Cholangitis)
	PBC (Primary Biliary Cholangitis)
	MELAS (Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like Episodes) (Complex I Deficiency)
CR3053	LHON dry AMD / MASH / FA
CR3 series	CNS diseases Muscular diseases
CR4 series	Liver diseases Kidney diseases

Open Collaboration

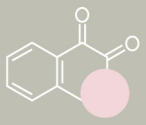
Covaltt and Curome Bioscience are companies advancing therapeutic drug development and brand-building in medical aesthetics, with Coenzyme K research as their core asset.

COVALTT | CUROME BIOSCIENCES

Coenzyme K is a proprietary quinone-based molecule with global exclusivity, developed and secured via the MITODAC platform

NAD+ Enhancement Compound COENZYME K

Coenzyme K

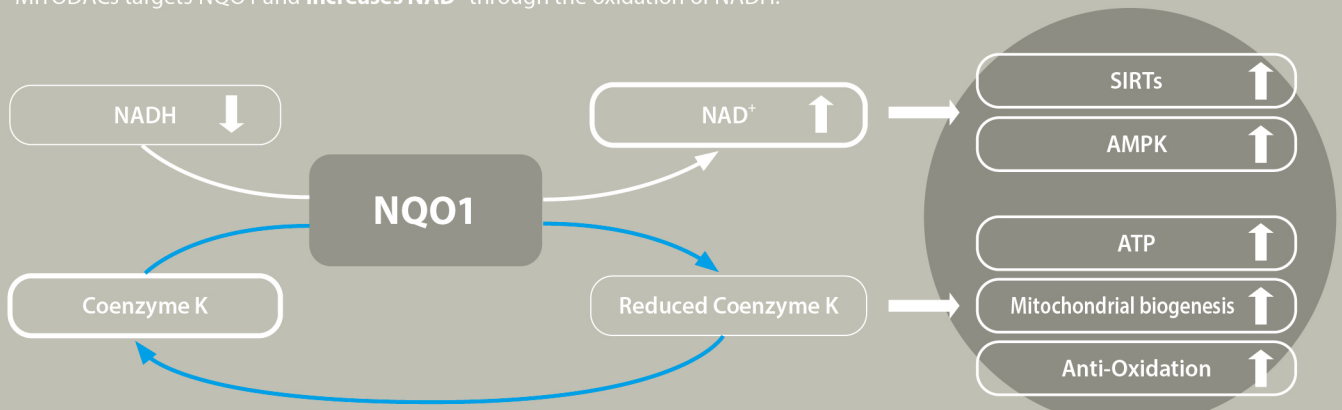


Quinone-based Coenzyme K core structure

Variable substituent design enables precise modulation of intracellular redox cycling and NAD+ recovery

MoA of Coenzyme K

MITODACs targets NQO1 and **increases NAD+** through the oxidation of NADH.



NQO1: NAD(P)H quinone oxidoreductase 1

01. Coenzyme K targets NQO1, oxidizing NADH and directly increasing intracellular NAD+ levels.
02. This process reactivates the NAD+/NADH redox cycle without consuming external energy.
03. The elevated NAD+ activates sirtuins and AMPK, restoring cellular metabolic regulation and stress-response capacity.
04. At the same time, ATP production is enhanced, leading to an overall improvement in cellular energy status.
05. As a result, mitochondrial biogenesis is increased, antioxidant capacity is strengthened, and NAD+/ATP-driven functional recovery is achieved.

"NAD+ Redox Loop ON"

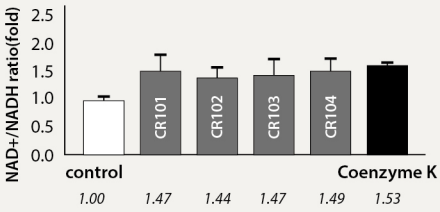
Cellular Function Restored Through Redox Loop Activation

NAD+ Enhancement Compound COENZYME K

Increase in NAD+

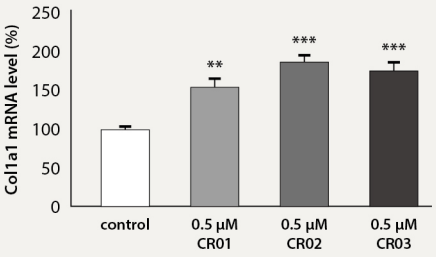
Improved NAD+/NADH Ratio

· A549 human lung carcinoma cell line
· Coenzyme K compounds 5
· 1 μM, 30 min

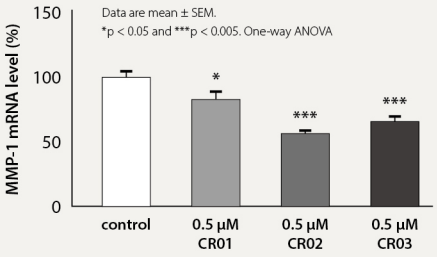


ECM Restoration

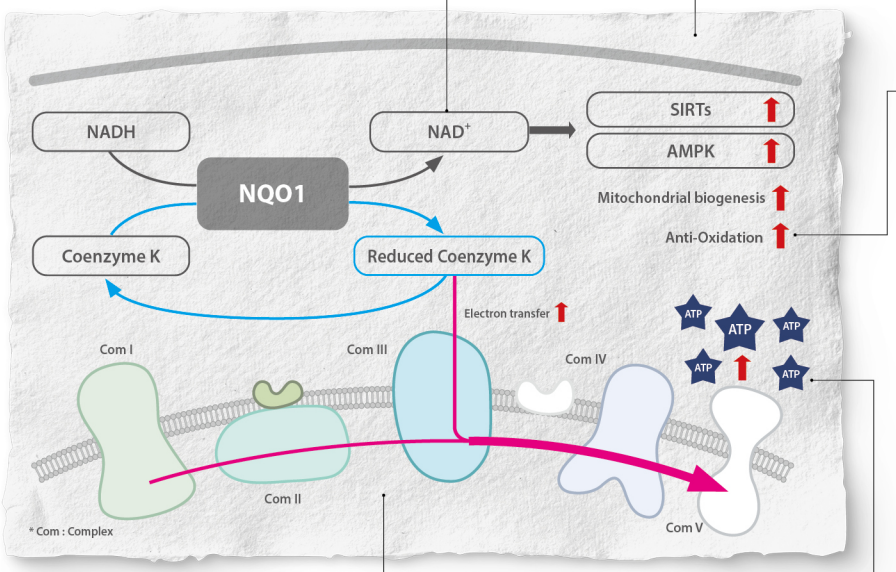
· HaCaT human keratinocyte cell lineThree
· Coenzyme K compounds
· 0.5 μM · 24 h
· Real-time quantitative PCR (qPCR)



▶ Collagen 1A1 (Col1A1) mRNA Expression



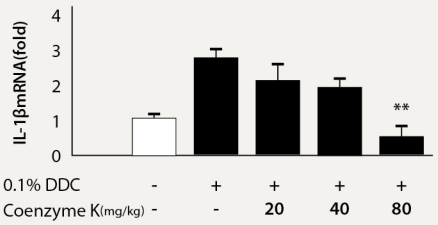
▶ Matrix metalloproteinase-1 (MMP-1) mRNA Expression



Improvement of ROS levels

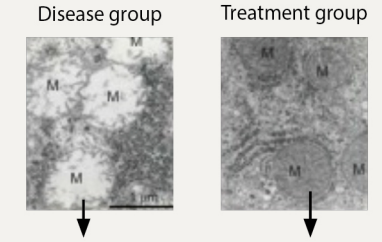
Suppression of inflammatory responses

· PSC Mouse Liver Tissue
· Dose-dependent administration for 1 week



Restoration of mitochondrial function

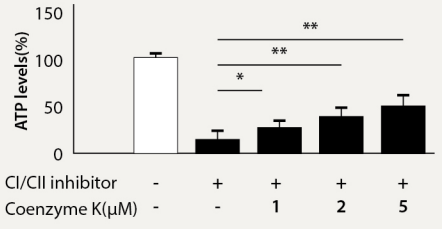
· DIO Mouse Liver Tissue
· Coenzyme K at 50 mg/kg
· Administered for 8 weeks



Increase in ATP

Cellular Energy Supply in Skin Cells

· Complex I/II–Inhibited Cell Model
· Treatment for 30 minutes at varying concentrations



[Ref.]
· Pharmacological stimulation of NADH oxidation ameliorates obesity and related phenotypes in mice (2009, Diabetes)
· SIRT2 regulates tumour hypoxia response by promoting HIF-1α hydroxylation (2015, Oncogene)
· KL1333, a Novel NAD+ Modulator, Improves Energy Metabolism and Mitochondrial Dysfunction in MELAS Fibroblasts (2018, Front Neurol.)
· Beta-lapachone ameliorates the progression of primary sclerosing cholangitis pathogenesis in rodent models (2024, Life Sciences)
· Internal experimental data (MITODAC Platform)

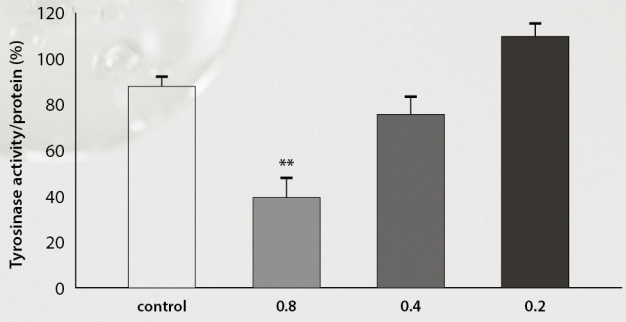
"Coenzyme K Restores Skin Cell Function"

Reactivating Core Skin Cell Functions Through NAD+ Redox Recovery

Inhibition of melanin production

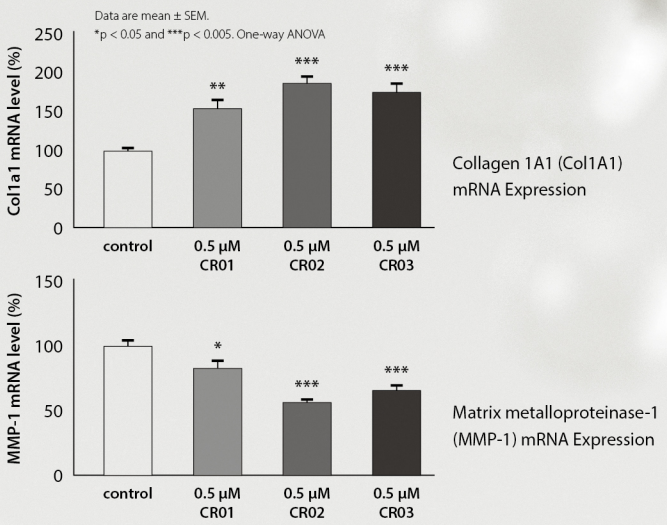
Tyrosinase activity

· Control group: untreated (no test compound)
· Treatment groups: Coenzyme K at 0.8 μM, 0.4 μM, and 0.2 μM



Increased Collagen

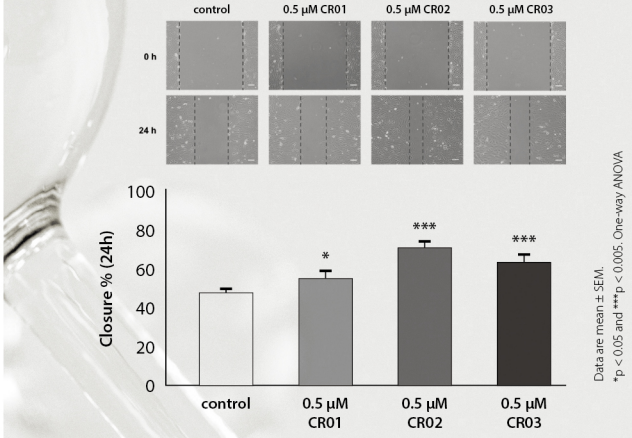
· Cell Line: HaCaT human keratinocyte cell line
· Test Compounds: Three Coenzyme K compounds
· Treatment Concentration: 0.5 μM
· Treatment Duration: 24 h
· Analysis Method: Real-time quantitative PCR (qPCR)



Wound healing

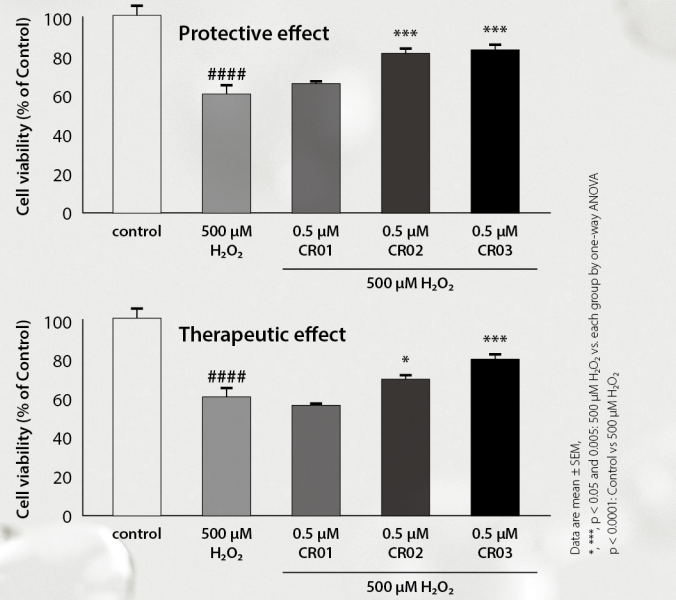
Evaluation of HaCaT cell migration and wound healing capacity

· Cell Line: HaCaT human keratinocyte cell line
· Assay: Scratch-based wound healing assay
· Control: Untreated (no test compound)
· Treatment Groups: Three Coenzyme K compounds, each at 0.5 μM
· Observation Time Points: Immediately after scratching (0 h) and 24 h post-scratch
· Evaluation: Wound closure (%) was calculated based on the reduction in the scratch gap.



Reduced Inflammation

· CelLine: HaCaT human keratinocyte cell line
· ROS Inducer: Hydrogen peroxide (H_2O_2), 500 μM
· Test Compounds: Three Coenzyme K compounds
· Treatment Concentration: 0.5 μM



[Ref.] Internal experimental data (MITODAC Platform)

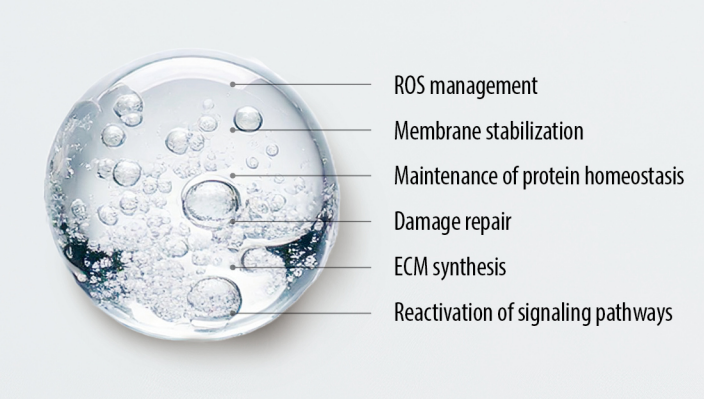
NAD+ Recovery, Inside the Cell

NAD+ enhancement compound

héjeuna | Specification

Active ingredient	Coenzyme K concentration	1 μM
	Coenzyme K molecular mass	242 Da
Contextual ingredients	HA concentration(2.5 Mda)	25 mg/vial
	PDRN concentration	50 mg/vial
	Glutathione(GSH) concentration	7.5 mg/vial
Appearance	Appearance : a slightly translucent liquid with mild viscosity.	
Sterilization	steam sterilization (autoclave)	
Volume	5mL	
Expiry Date	36 months	
Packing	1vial/box	

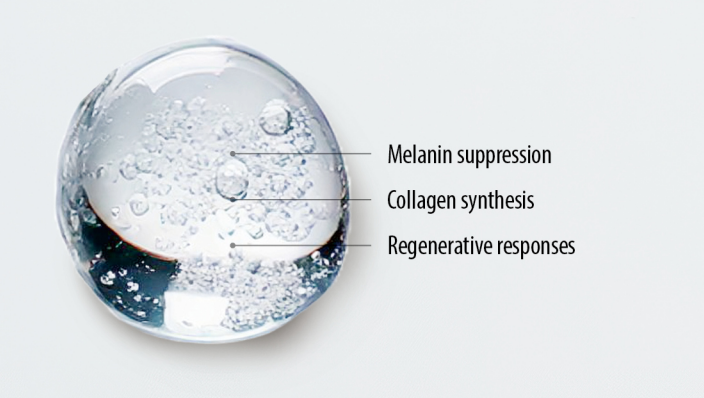
Context compounds do not create effects, they are designed to prevent those effects from being dispersed



Concurrent Multirole Demands in Cellular Functional Recovery

As Coenzyme K rapidly restores the cellular loop within seconds to hours, cells initially face multiple simultaneous functional demands.

All of these are legitimate demands,and none of them are unnecessary.



At the initial stage, focus on the intended functions is required

This is not due to a lack of energy, but because multiple demands arise simultaneously.In this early state, energy cannot be concentrated on the intended functional responses.

What Do Context Compounds Do?

Context compounds are auxiliary components designed to absorb the initial environmental burdens that arise immediately when cellular function is restored by Coenzyme K, including ROS, membrane instability, and non-specific energy consumption. By organizing these chaotic early responses, they ensure that the restored cellular energy is preferentially directed toward intended functional outcomes. Once this stabilizing role is fulfilled, the context compounds are designed to be consumed and dissipated.

> Héjeuna's context compounds are consumptive auxiliary components that prevent the cellular energy restored by Coenzyme K from being dispersed during the initial response phase.

Supplementing NAD+ is not the same as restoring its function

NR, NMN, and NAD+ -based skin boosters rely on an extracellular supplementation approach to increase NAD+ levels and therefore fall within the same **"supplementation paradigm"** as conventional ECM-centered skin boosters. Rather than directly restoring the metabolic and redox imbalances that underlie cellular functional decline, this approach primarily focuses on temporarily increasing the intracellular availability of specific molecules. As a result, when compared with more fundamental and efficient anti-aging strategies that presuppose the restoration of the intracellular NAD+ redox loop, these approaches exhibit inherent **structural limitations**.

Inefficiencies of NR, NMN, and NAD+ Supplementation Approaches

Multiple Prerequisites Required for Intracellular Function

For NR, NMN, and NAD+ to exert intracellular activity, multiple prerequisites must be met simultaneously, including cellular uptake, enzymatic conversion, adequate cellular energy status, and substrate availability. NMN and NAD are hydrophilic, highly polar, and relatively large molecules, making direct transmembrane passage inefficient. Although NR exhibits comparatively higher membrane permeability, it must undergo multiple enzymatic conversion steps to be transformed into NMN and subsequently NAD+ within the cell. The efficiency of these processes is highly dependent on cellular conditions and is therefore intrinsically constrained.

Importance of the NAD+/NADH Ratio over Absolute NAD+ Levels

The critical indicator of cellular functional recovery is not the absolute increase in NAD+ levels, but rather the change in the NAD+/NADH ratio. This ratio serves as a key signal regulating metabolism, mitochondrial function, and the activation of gene regulatory pathways. Consequently, an increase in NAD+ that is not accompanied by a corresponding reduction in NADH is unlikely to result in meaningful functional restoration.

Structural Differences between One-Time Supplementation and Redox Cycle–Based Mechanisms

The significance of NAD+ in cellular functional recovery lies in the fact that the NAD+/NADH balance reflects the status of NQO1-mediated redox cycling and electron flow.However, simple supplementation strategies using NR, NMN, or NAD+ are limited in that the supplemented molecules are ultimately consumed or lost through metabolic processes, without being efficiently integrated into a cyclic system that transfers electrons to the electron transport chain and drives ATP production.
In contrast, Coenzyme K–based molecules can repeatedly participate in NQO1-mediated redox cycling as long as cellular conditions are maintained. This confers a mode of action that is qualitatively distinct from mere increases in NAD+ concentration, enabling sustained engagement with cellular redox and energy metabolism.

Category	NR, NMN, NAD+	Coenzyme K
Core Approach	Extracellular supplementation of NAD+ or its precursors	Direct activation of intracellular redox cycling
Conceptual Classification	ECM-based supplementation approach	ICM-based functional restoration approach
Cell Membrane Permeability	Limited, dependent on transporters and conversion enzymes	Small-molecule structure with direct intracellular action
Required Conditions	Multiple prerequisites, including membrane transport, enzymes, ATP, and substrate availability	Primarily dependent on NQO1 activation
Mode of NAD+ Increase	Focused on increasing absolute NAD+ levels	Based on conversion of NADH to NAD+
Key Indicator	NAD+ concentration	NAD+/NADH ratio
Link to Energy Metabolism	Indirect and inefficient	Directly coupled to electron flow
Duration of Action	Consumed and depleted after use	Repeated action sustained under redox cycling conditions