Anallerg®-NAD

INCI： Nicotinamide adenine dinucleotide

CONTENTS

01 Background

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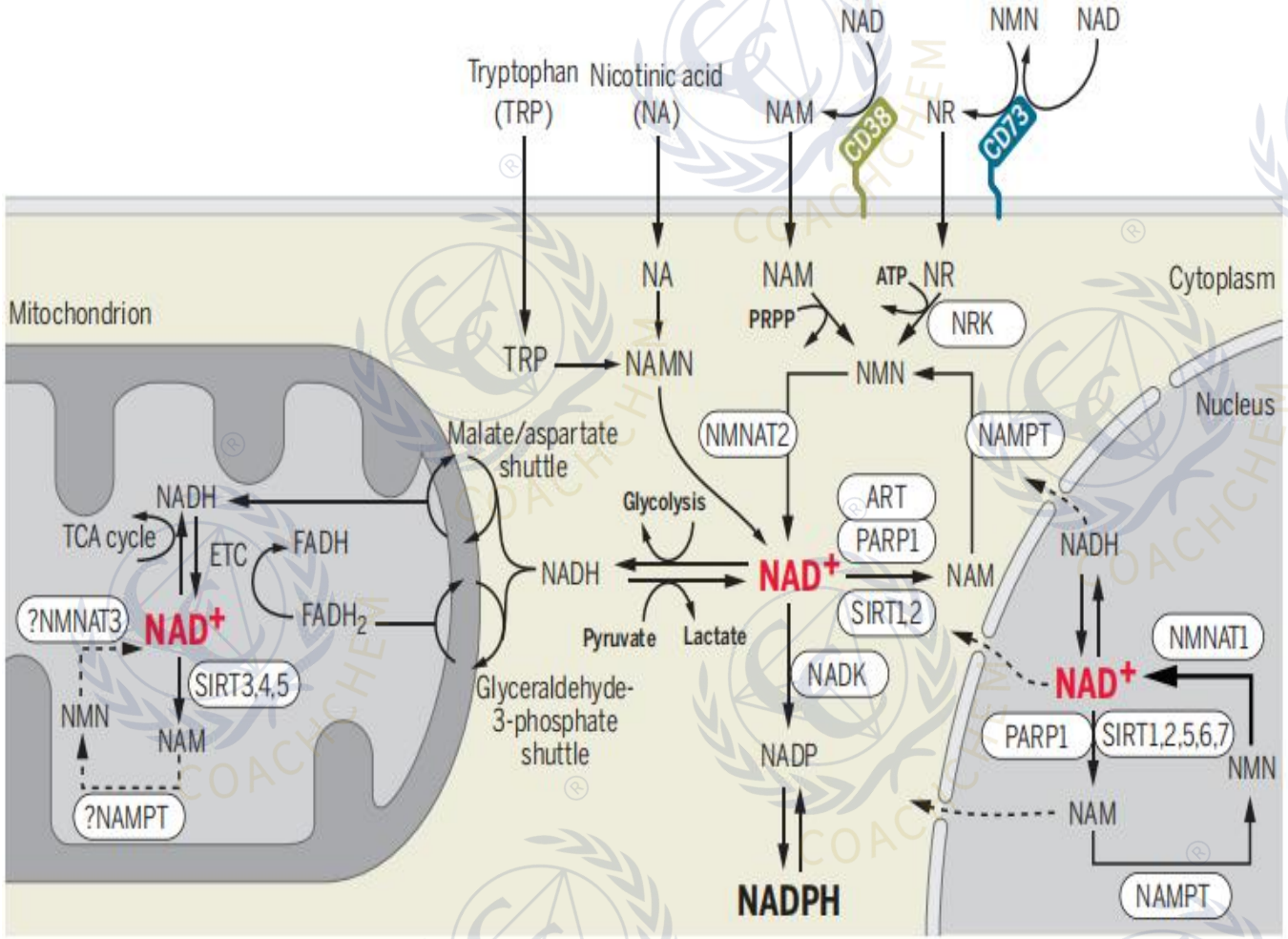
Background introduction of NAD+

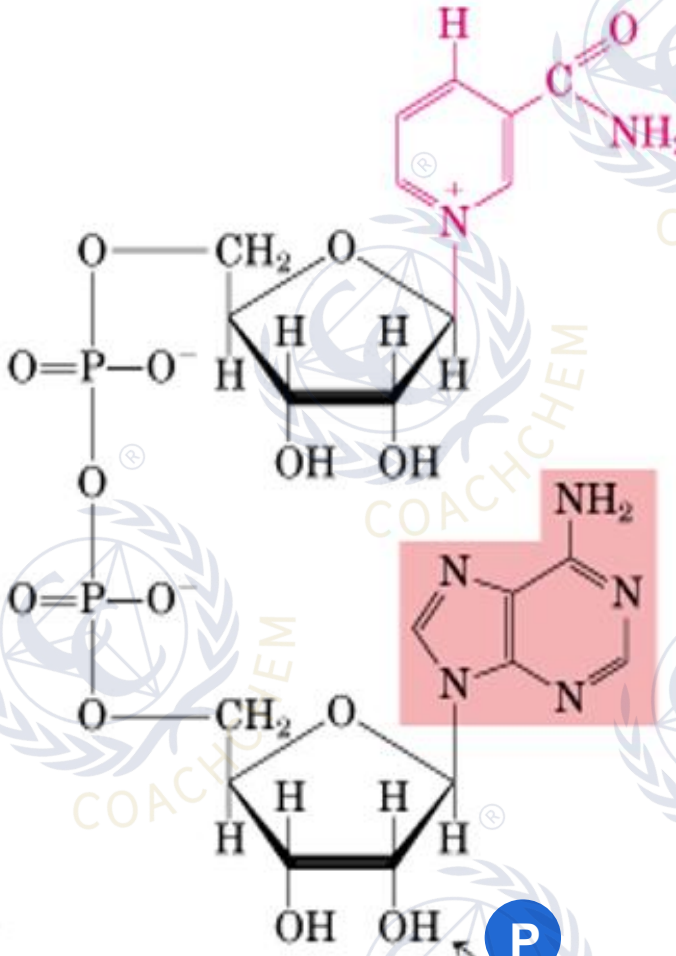


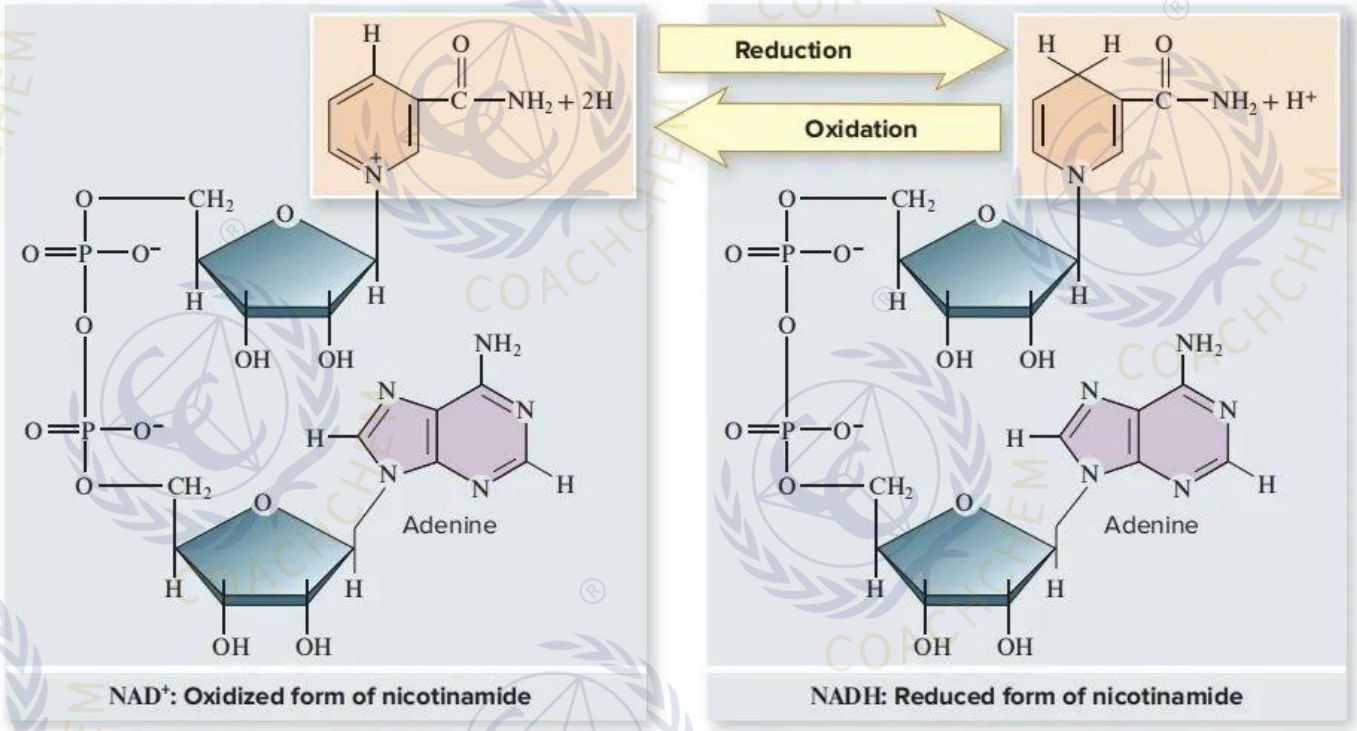
Eric Verdin. (2015). Special Section 350（6265）: 1208-1213.

- Various intracellular NAD+ precursors, including tryptophan, niacin, nicotinamide, nicotinamide riboside（NR）, and β-nicotinamide mononucleotide（NMN）, undergo extracellular metabolism mediated by enzymes like CD38 and CD73.
- NAD+ is essential for energy generation, transferring reducing equivalents either through glycolysis or in the form of NADH from the tricarboxylic acid cycle.
- The pivotal role of NAD+ in mitochondrial intermediary metabolism suggests that changes in mitochondrial NAD+ levels may impact metabolic efficiency, aging, and age-related diseases.
- NAD+ serves as a precursor to NADPH, essential for the synthesis of various lipids, including ceramide, and acts as a reducing agent for cellular antioxidants.

Anallerg®-MN

Background introduction of NAD+





NAD+ is the oxidized form of NAD, which converts into NADP, helping the cell's metabolism and energy conversion function.

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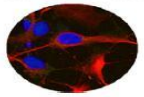
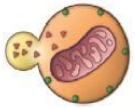
Background introduction of NAD^+

Hallmarks of aging	Pathways and conditions affected by changes in NAD^+ levels	Refs
Genomic instability 	↑ NAD^+ levels lead to ↑ DNA repair capacity; ↓ NAD^+ leads to ↑ ROS accumulation	[11,14,38,55]
	Mutations in DNA repair genes associated with premature aging disorders (e.g., XPA and CS), lead to ↓ NAD^+, PARP1 hyperactivation, neurodegeneration, and mitochondrial dysfunction	
	SIRT1 interacts with DNA repair enzymes Ku70, PARP1, and WRN. PARP1 is involved in both BER and NER; SIRT3 enhances NHEJ and HR via interaction with PARP1	
Telomere attrition 	Data not available	
Epigenetic alterations 	Treatment with NAD^+ precursors NR and NMN activates SIRTs, which deacetylate and activate transcription factors, including PGC-1α, FOXOs, and others, all related to aging	[8,9,44,49,59]
	PARP1 may be involved in chromatin structure modulation and insulation promotion, associated with changes in gene expression. Also, PARP-1 may function as a transcriptional co-factor. PARP-2 transcriptionally regulates SIRT1, indirectly connecting NAD^+ levels to epigenetic alterations	
Stem cell exhaustion 	NR treatment rejuvenated muscle, neuronal, and melanocyte SC pools through induction of UPR^{mt} and synthesis of prohibitin proteins; leads to ↑ oxidative respiration and/or ATP levels and higher mitochondrial membrane potential	[45,76]
	NR treatment prevented senescence of muscle SC in mouse model of muscular dystrophy	
	SIRT1 maintains naïve state of pluripotent SC by deacetylating Oct4. Restoration of NAD^+ in aged somatic cells (overexpression of NNT or NMNAT3) enhanced reprogramming efficiency and prolonged lifespan of mesenchymal SC by delaying senescence	
Loss of proteostasis 	NAD^+ precursor NR, or PARP1 inhibitors, activate UPR^{mt}, causing translocation of FOXO transcription factors, triggering ↑ antioxidant defenses in mice and worms, prolonging lifespan and health. UPR^{mt} activation also observed in yeast	[26,38,39,44,59]
	NR treatment of an AD mouse model (Tg2576) ↑ NAD^+ levels and PGC-1α-mediated degradation of Bace1 leading to ↓ Aβ production. AD mice crossed with CD38 KO mice showed attenuated AD pathology, suggesting that ↑ NAD^+ leads to ↓ aggregated dysfunctional proteins, such as Aβ	

Hallmarks of aging	Pathways and conditions affected by changes in NAD^+ levels	Refs
	NR ↓ senescence in both neuronal and melanocyte SC by improving mitochondrial function, dependent on SIRT1 function	
	↑ NAD^+ (overexpression of NNT and NMNAT3) delays senescence in mesenchymal SC	
Comprised autophagy 	Exogenous NAD^+ administration ↑ autophagy in retinal pigment epithelium	[105]
	↑ NAD^+ synthesis, caused by AMPK activation through SIRT1/mTOR activation, leads to induction of autophagy in senescent cells	

Hallmarks of aging	Pathways and conditions affected by changes in NAD^+ levels	Refs
Mitochondrial dysfunction 	Mouse and worm models of XPA, CS, and A-T show impaired mitophagy and mitochondrial biogenesis, likely due to ↓ activity of NAD^+-SIRT1-PGC-1α axis. These defects can be restored by ↑ NAD^+ with NAD^+ precursors	[14,40,49,50,84]
	↑ NAD^+ in aged mice restores mitochondrial function to that of young mice in a Sirt1-dependent manner either via PGC-1α/β or AMPK	
	↓ NAD^+ leads to ↓ TFAM signaling, likely via HIF-1α stabilization, resulting in ↓ mitochondrial biogenesis and loss of mitochondrial homeostasis. Short-term treatment with NMN ↑ NAD^+ and restored mitochondrial homeostasis in mice via Sirt1-PGC-1α activation	
Deregulated nutrient sensing 	NAD^+ levels affected in DIO. NR treatment can help to prevent high-fat DIO by ↑ NAD^+ and stimulating SIRT1 activity	[9,40,49,50,84]
	NNMT deficiency protects against DIO by ↑ SAM and NAD^+ in adipose and liver. Beneficial effects of calorie restriction are lost when SIRT1 and SIRT3 are inhibited	
	NMN treatment of a diabetes mouse model ameliorated glucose intolerance and ↑ hepatic insulin sensitivity or secretion by restoring NAD^+ levels (likely due to ↑ SIRT1 activity)	
	NR/NMN treatment of mice fed a HFD ↑ use of lipids as substrates, ↑ energy expenditure, and improved insulin sensitivity	
Altered cellular communication 	NR treatment prevented noise-induced hearing loss and led to regeneration of neurite ganglia mediated by NAD^+-dependent SIRT3 activity. ↑ NAD^+ directed SIRT1 activity delays axon degeneration	[25,40,50,72]
	NMN treatment reversed age-related changes in expression of genes related to inflammation, partly by increasing SIRT1 activity. Parp1 KO mice, CD38 KO mice, and NNMT KO mice exhibit ↑ NAD^+ levels and SIRT1 activation, correlating with ↓ risk of high-fat DIO	
Cellular senescence 	NAD^+ concentrations ↓ during senescence	[8,45,47]
	NAD^+ levels ↓ in aged human tissues, resulting in changes in oxidative stress and cellular metabolism, suggesting link between NAD^+ metabolism and senescence	
	pathology, suggesting that ↑ NAD^+ leads to ↓ aggregated dysfunctional proteins, such as Aβ	

Abbreviations: BER, base excision repair; DIO, diet-induced obesity; KO, knockout; mt, mitochondrial; ROS, reactive oxygen species; SAM, *S*-adenosyl methionine; SC, stem cell; UPR, unfolded protein response; ↑ increase; ↓ decrease.

NAD^+ plays a vital role in repairing DNA, reducing oxidative stress, restoring mitochondrial function, and maintaining telomere length, closely linking it to the aging process.

Sultani G, et al. Epithelial-mesenchymal tr[J]. Cancer & metabolism, 2016, 4(1): 1-13.

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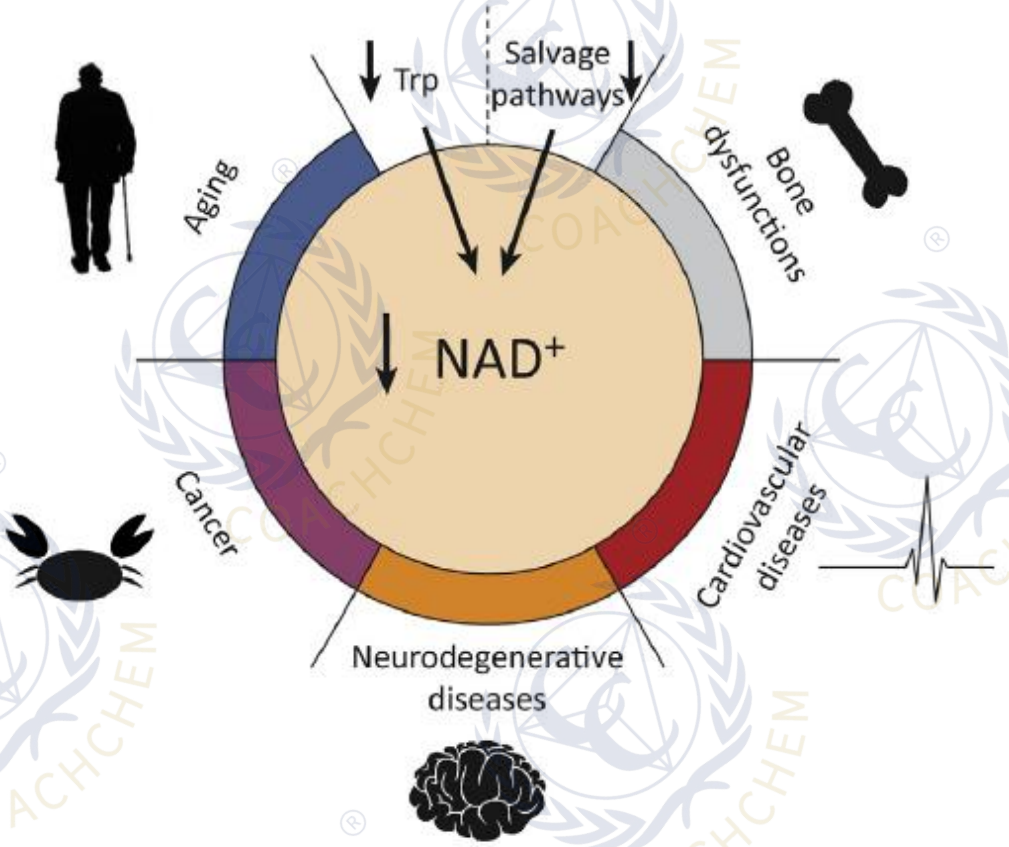
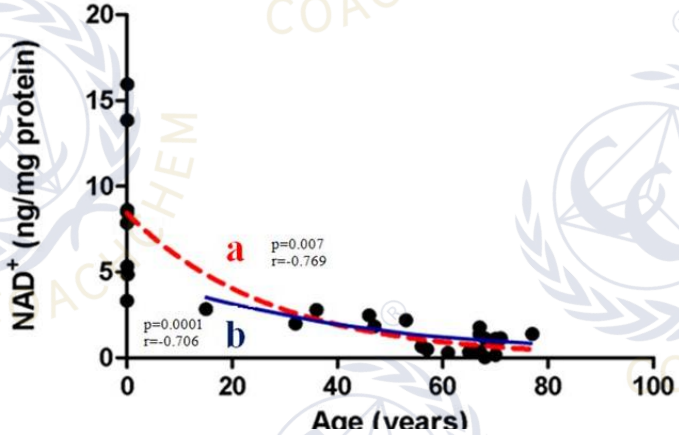
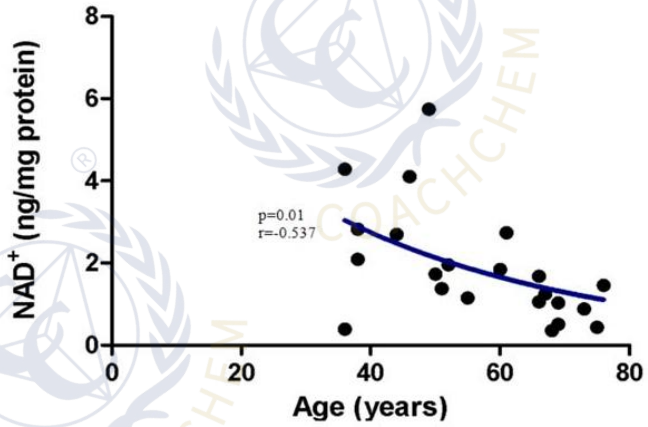
Background introduction of NAD+



Garrido A, Djouder N. [J]. Trends in cancer, 2017, 3(8): 593-610.





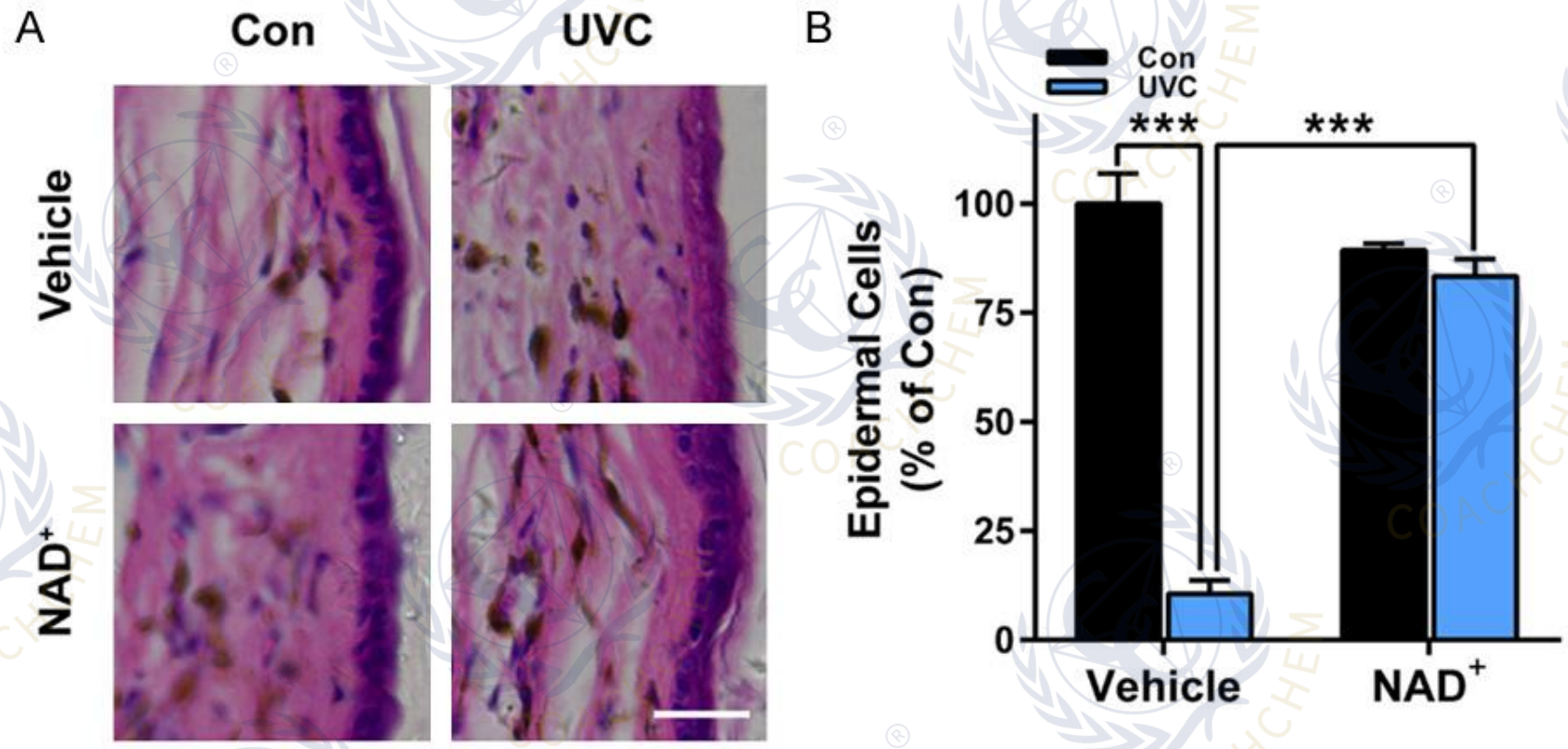
Massudi H, et al. [J]. 2012.

In middle age, intracellular NAD+ levels drop to half ,potentially contributing to age-related aging and diseases

02 Mechanism & Efficacy

Anallerg®-NAD Anti-Photodamage

➢ UV Damage Protection

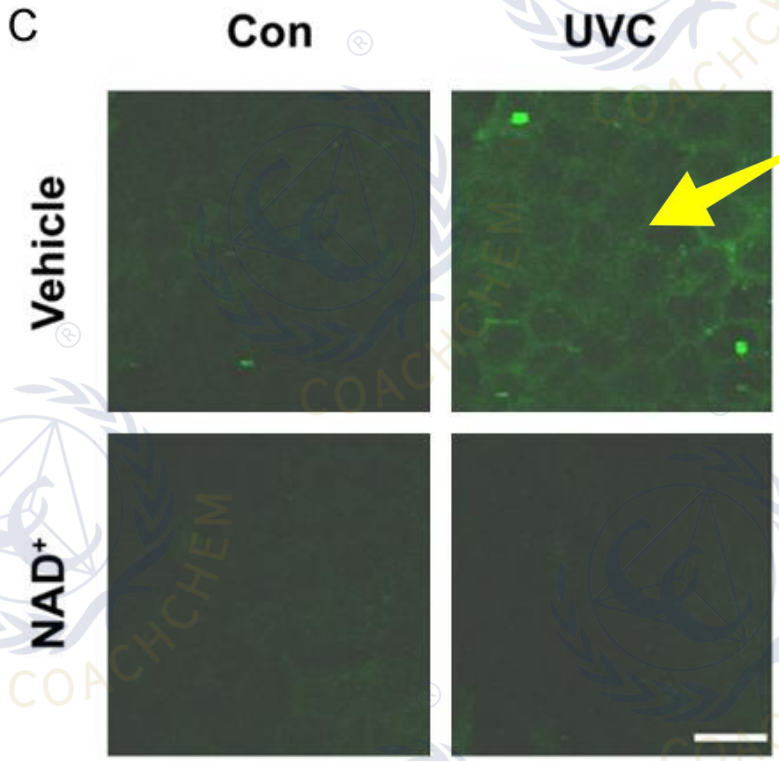


NAD+ significantly reduced skin damage induced by UVC

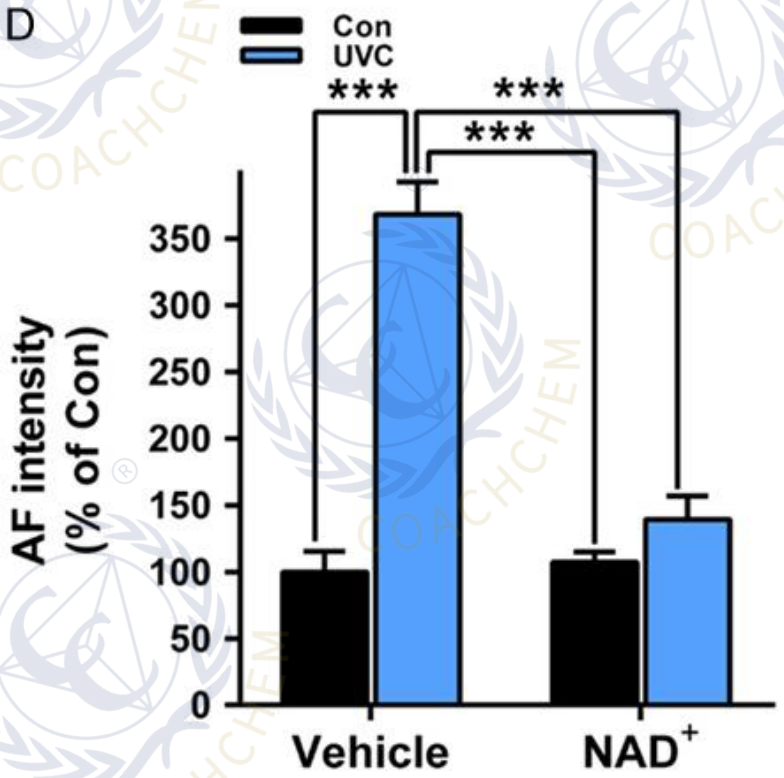
Li, Mengmeng, et al. *International Journal of Physiology, Pathophysiology and Pharmacology* 15.2 (2023): 41.

Anallerg®-NAD Anti-Photodamage

➢ UV Damage Protection



UVC-induced skin **green fluorescence (AF)** is correlated with the skin damage



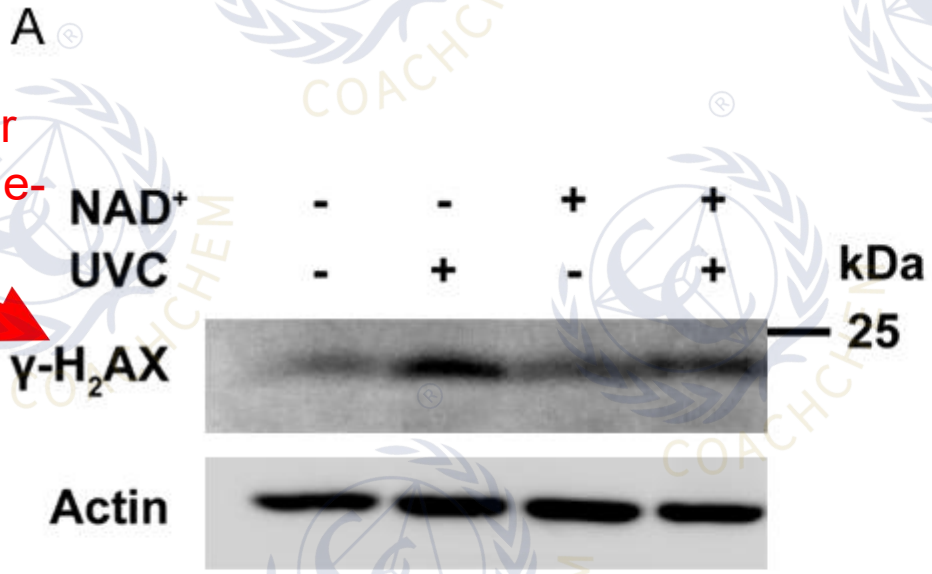
NAD+ markedly decreased the increase in green AF intensity from UVC-induced skin damage

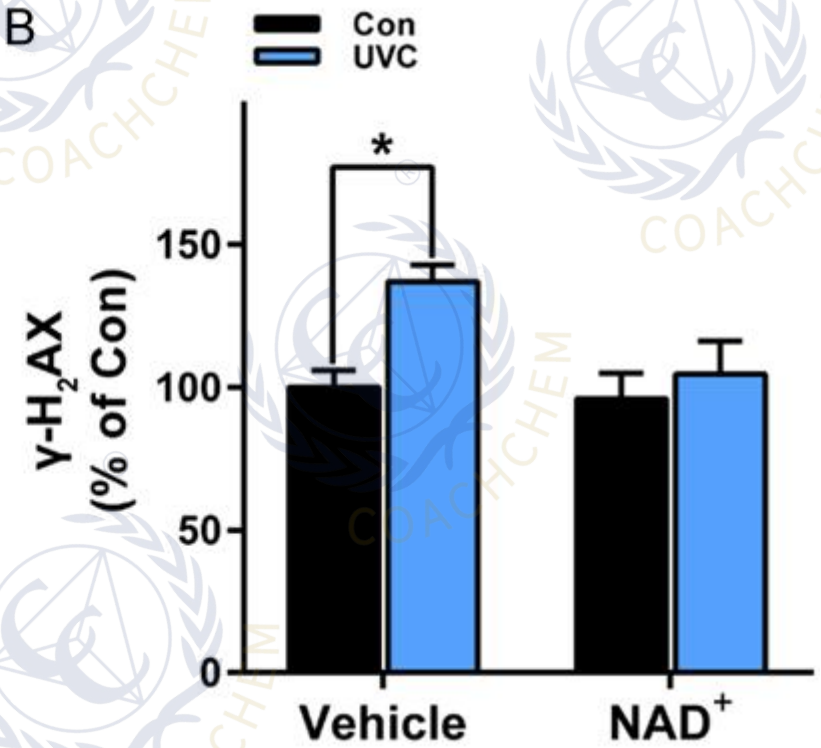
Li, Mengmeng, et al. *International Journal of Physiology, Pathophysiology and Pharmacology* 15.2 (2023): 41.

Anallerg®-NAD Anti-Photodamage

➢ DNA Protection from UV Damage

γ-H2AX is a molecular marker for DNA double-strand breaks



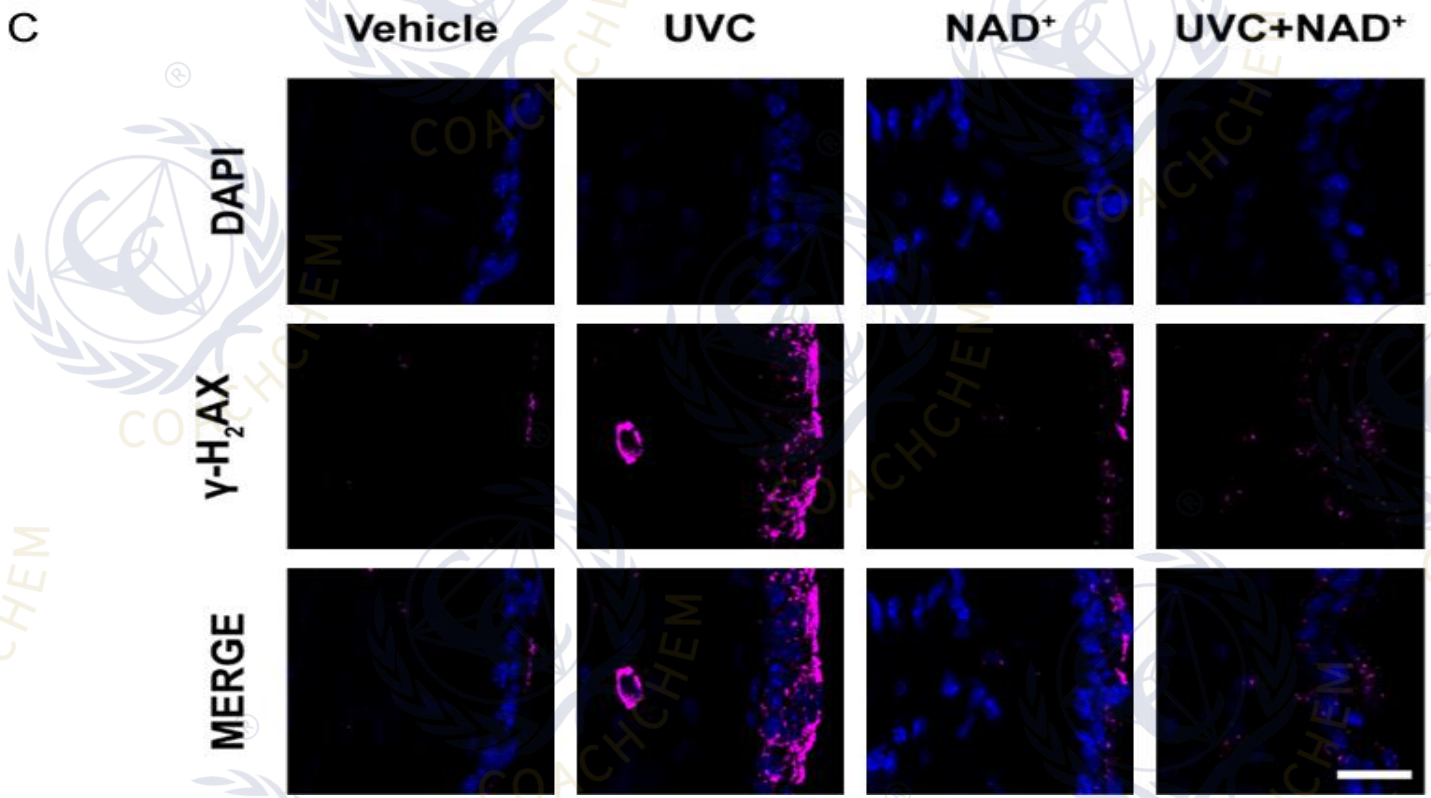


NAD+ significantly reduced UVC-induced skin sDNA damage

Li, Mengmeng, et al. *International Journal of Physiology, Pathophysiology and Pharmacology* 15.2 (2023): 41.

Anallerg®-NAD Anti-Photodamage

➢ DNA Protection from UV Damage



NAD+ significantly reduced UVC-induced skin sDNA damage

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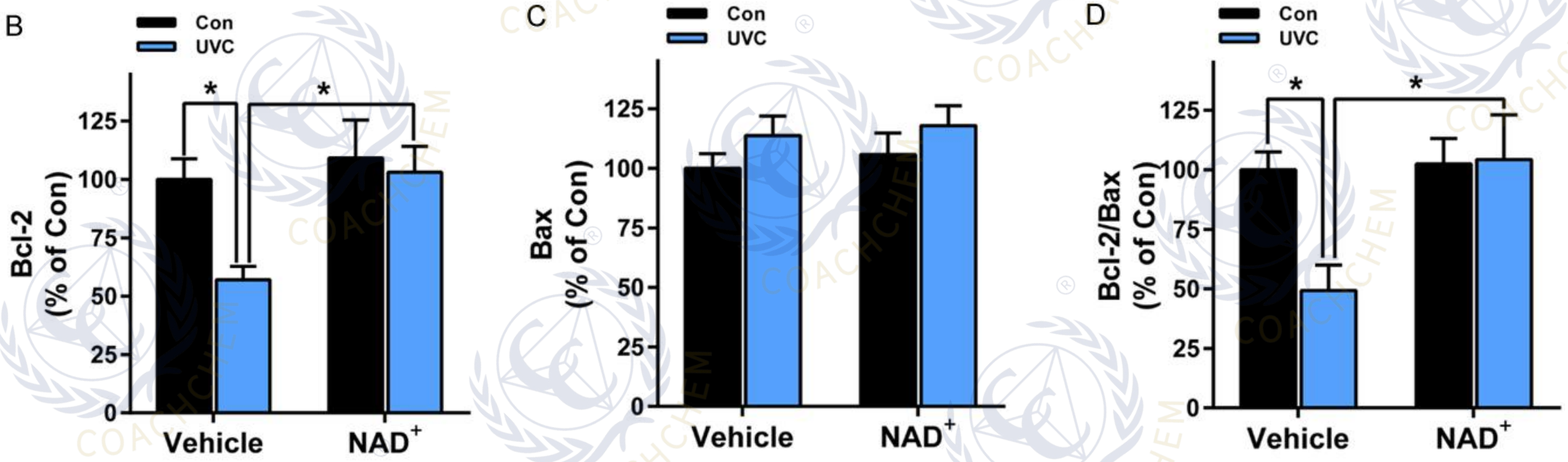
Anallerg®-NAD Anti-Photodamage

➢ Reduction of UV-Induced Apoptosis



NAD+ notably mitigated the decrease in the Bcl-2/Bax ratio caused by UVC, reducing skin cell apoptosis

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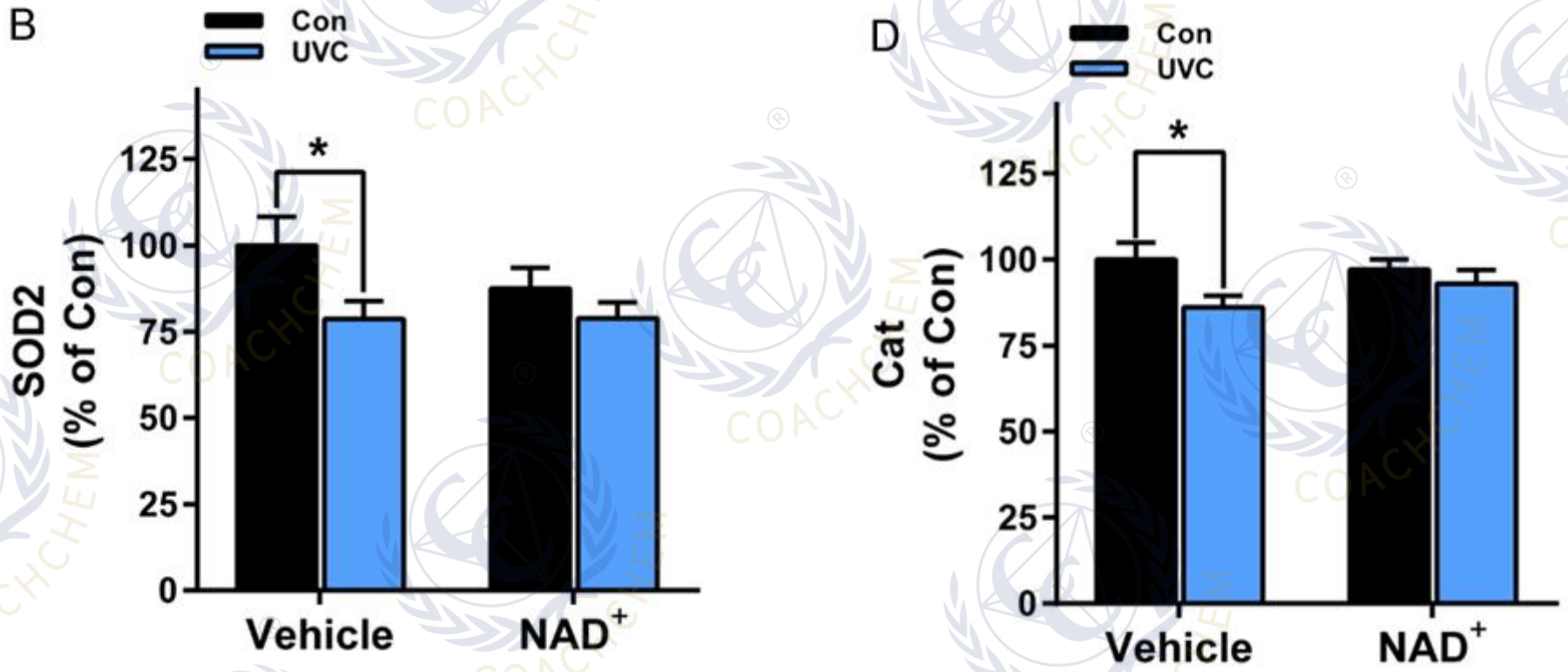
Anallerg®-NAD Anti-Photodamage

➢ Resistance to UV-Induced Oxidative Stress

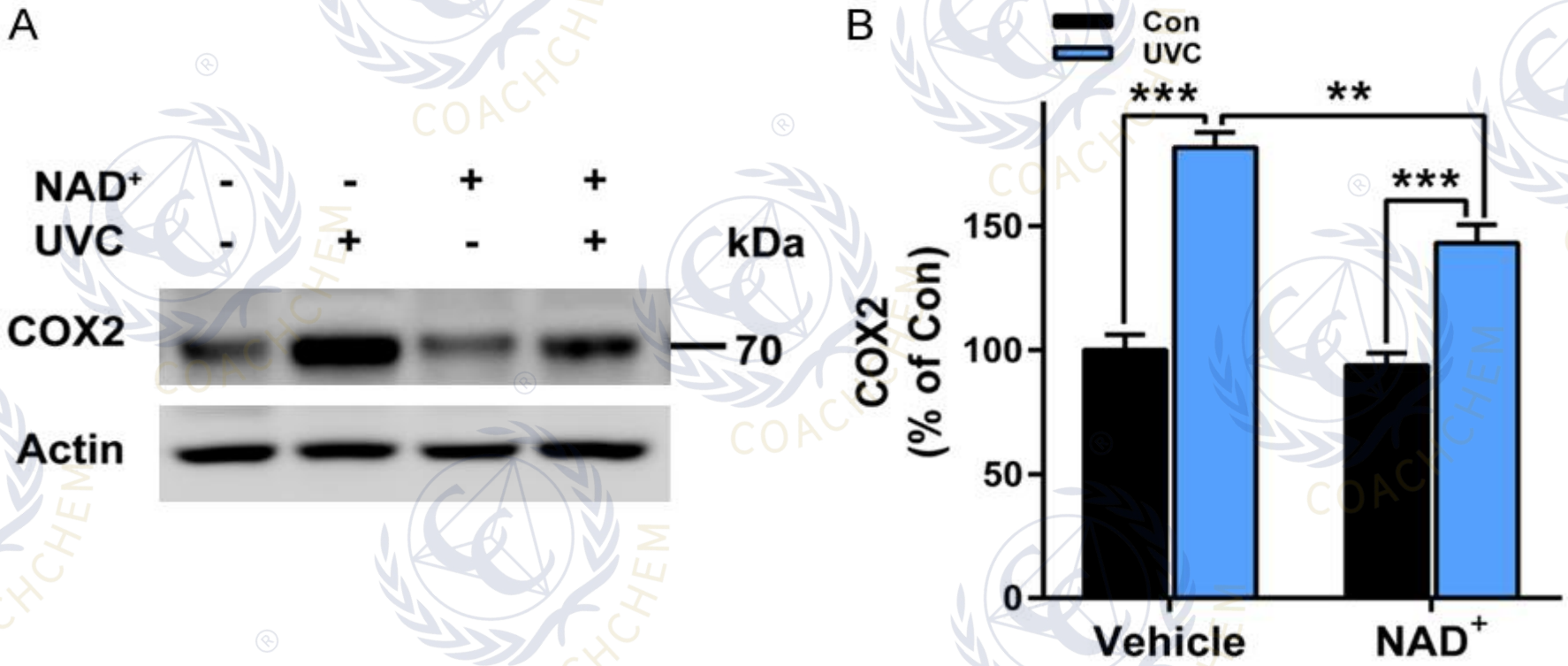


NAD+ significantly lessened the decline in mitochondrial superoxide dismutase (SOD2) and catalase (CAT) levels induced by UVC

Li, Mengmeng, et al. *International Journal of Physiology, Pathophysiology and Pharmacology* 15.2 (2023): 41.

Anallerg®-NAD Anti-Photodamage

➢ Resistance to UV-Induced Inflammatory Response



NAD+ effectively inhibited the increase in inducible cyclooxygenase (COX2) levels caused by UVC in the skin

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Anallerg®-NAD Efficacy Summary

- **Maintains normal energy metabolism and mitochondrial function** in skin, preserving elasticity and radiance while preventing skin laxity and wrinkles
- **Helps skin cells resist damage from UV rays and other environmental stressors**, preventing premature aging.
- **Acts as a key coenzyme for Sirtuins (longevity proteins)**, assisting skin cells in maintaining normal growth and differentiation to prevent skin issues.
- **Participates in the activity of PARP (poly(ADP-ribose) polymerase)**, aiding in the repair of skin cell damage.

03 Product Introduction

Anallerg®-NAD

- INCI: Nicotinamide Adenine Dinucleotide
- Appearance: White to off-white powder
- Purity: >98%
- Recommended Usage: 0.1% - 5.0%
- Application: Recommended to be added at low temperatures below 40°C; suitable for creams, lotions, serums, etc.
- Storage Recommendations: Store in a cool, dark place; keep sealed at 2-8°C


COACHCHEM
THANKS