

Coenzyme-1 (NADH) Cannot Prevent Death But It Can Extend Lifespan

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Coenzyme-1 is biochemically Nicotinamide-Adenine Dinucleotide Hydride, abbreviated as NADH. It was discovered in 1903 as an important co-factor for the fermentation of alcohol by yeast. In this more than 100 years since its discovery NADH has been found to be essential for more than 1000 metabolic reactions. The five most important are :

- (1) NADH is the fuel for the energy production in every cell.
- (2) NADH repairs damaged cells and DNA.
- (3) NADH is a highly potent antioxidant.
- (4) NADH improves the cellular immune system.
- (5) NADH stimulates adrenaline and dopamine.
- (6) NADH enhances NO production.

NADH is the fuel for the energy production in the cell

As the biological form of hydrogen, NADH reacts with the oxygen present in every cell and produces energy and water. The energy is stored in form of the chemical compound AdenosineTriPhosphate, abbreviated to ATP. ATP is the life energy of every living cell. If the ATP level of a cell falls below a critical threshold then the cell dies off. The decisive question is : Can we increase the ATP production in the cells of our body? The answer is- yes we can, utilising NADH.

This effect of NADH was demonstrated by studies performed at the University of Graz in Austria. When heart cells are incubated with NADH a 30% increase of ATP in these cells was observed (1). Due to this increase in ATP energy the lifespan of these heart cells was more than doubled. This cell system allows to test other coenzymes and substances for their potential energy increasing effect.

From all the substances tested so far including NAD⁺ (the oxidized form of NADH), nicotinamide (vitamin B3), coenzyme Q10, creatine, carnitine and caffeine, only NADH increases ATP production in these cells. These experiments provide scientific proof that NADH can pass the cell membrane and can increase the ATP level in the cell by about 30%. With more ATP the cell can produce components essential for its functionality to a greater extent. Due to this effect the cells function better and live longer.

NADH repairs damaged cells and DNA

DNA mutations are the biochemical cause of numerous diseases such as diabetes, muscular dystrophy, cancer, arteriosclerosis, immunodeficiencies, rheumatoid arthritis, just to mention a few. Mammals have developed a DNA repair system, capable of repairing altered or damaged DNA. This DNA repair system needs NADH as an essential co-factor. In a number of research studies Professor Jiren Zhang, Chairman at the Department of Oncology at the University in Guangzhou, China, demonstrated that NADH can repair DNA damaged by the cytotoxic substances such as Doxorubicin or Cisplatin, which are frequently used as chemotherapeutic agents for the treatment of cancer-patients. The mechanism of the DNA repair by NADH is based on proteins such as Cyclin A, Cyclin B1, P53 and Bcl-2, all of which play a role in the regulation of the cell cycle (2). In addition, NADH has been shown to prevent apoptosis.

Based on this effect, NADH exhibits a protective effect for living cells. NADH is also able to revitalize damaged cells. When liver cells were exposed to a high almost lethal dose of X-rays their vitality decreased considerably and many of them died. When these cells were incubated with NADH about 70% of the damaged cells could be revitalized and regained full functionality. If these cells were incubated with NADH before exposure to radiation they could be protected from the damaging effect of radiation. The practical implications for the use of NADH in nuclear accidents such as the one happened some years ago in Fukushima are obvious.

NADH is also a very potent antioxidant

When too many free radicals evoked by pollution, smoking, alcohol, drugs, or other toxins attack the antioxidant protection shield of our body it becomes weak and ineffective. Damage to tissues and organs are the consequences. Hence it is of utmost importance to supply the organism with sufficient amounts of antioxidants against the attacks by free radicals. NADH regenerates also the antioxidative capacity of other compounds in the cell such as Coenzyme Q10 and Glutathione.

The antioxidative potential of NADH was proven by a double blind placebo controlled study at the University of Graz, Austria by giving NADH to young and healthy medical students (3).

NADH enhances the immune system

It was observed that NADH stimulates the biosynthesis of Interleukine-6 (IL-6). IL-6 has a neuroprotective effect and was found to be reduced in neurodegenerative diseases such as Alzheimer, Parkinson and Multiple Sclerosis (4).

NADH increases the production of adrenaline and dopamine

NADH leads (dosage dependent) to a six-fold increase of dopamine production. The enzyme tyrosine hydroxylase, responsible for dopamine biosynthesis, is enhanced by 70% (5). Due to this effect, NADH has a positive impact on the functions evoked by dopamine. This includes movement, coordination, power, concentration, cognitive performance also mood and well being. Dopamine has a stimulatory effect on all sexual functions particularly on libido.

NADH stimulates the production of Nitroxyde (NO)

Nitroxyde, abbreviated NO, exhibits features of a neurotransmitter. The most important effect of NO is relaxation of blood vessels. Due to this effect organs get more blood. NO is synthesized in our body by the enzyme 'NO-Synthase' from the amino acid L-Arginine. The coenzyme of the enzyme NO-Synthase is NADH. Therefore the more NADH the body has available the more NO can be produced. Professor Malinski from the University of Ohio has detected that NADH stimulates NO production in the cells to a much greater extent than all the other substances he had tested so far. Due to its blood vessel relaxing effect NADH is particular relevant for the treatment of angina, asthma, COPD and sexual dysfunction. The more NADH organs have available, they better they function and people live longer.

The therapeutic effect of NADH (Coenzyme-1) was discovered in 1987 by my late father and myself, when we infused NADH to a Parkinsonian patient, who showed the typical symptoms of this disease, tremor and small tripping steps. One hour after the infusion of 50 mg of NADH the patient's walking did improve remarkably. He could even jump. (www.youtube.com/watch?v=e2dPS8cx0Kc)

The approach from the intravenous form of NADH to a tablet of NADH took more than 4 years of intensive research, because NADH, as biological form of hydrogen, is a very sensitive substance which degrades rapidly even in dry state when blended with lactose the most common ingredient of drugs. The author succeeded in

stabilizing NADH and transposing it into a tablet form in which NADH is stable for at least 2 years, the requirement for an ethical drug. By using this stabilized NADH formulation numerous GCP studies have been performed in the U.S., as well as in Europe. In an FDA approved, double-blind placebo controlled study, it was found that NADH leads to an of certain cognitive functions in patients with Alzheimer dementia (6). Another FDA approved double-blind study with patients suffering from CFS, (Chronic Fatigue Syndrome) revealed more than 80% of CFS patients were relieved from their fatigue after a 6 month treatment period (7). NADH improves symptoms of other neurodegenerative ailments such as Parkinson's disease (8). Furthermore, NADH has been used for treatment of cancer patients under the aspect that most cancer cells exhibit an ATP deficiency and this lack of energy may be the cause of this disease. Since NADH can increase ATP energy in tumor cells, more than 70 patients with various types of cancer such as lung, prostate, mammary, brain tumors and lymphomas have been treated with NADH. Most of them are disease free or show no tumour progression (9).

NADH improves physical performance

Dr. Bill Misner, Coach of some top US athletes, observed that sprint as well as the endurance performance was significantly better after 60 days with a daily dose of 10 mg NADH. At the Institute for Sportsmedicine at the University of Freiburg, highly conditioned athletes obtained 30 mg NADH per day for 4 weeks. This treatment resulted in a reduction of oxygen consumption and an increase in the respiratory ratio at defined work-out (10). In addition, the lactate level under NADH treatment was lower than under placebo. The reduction of oxygen consumption under NADH indicates an improved utility of oxygen. This effect is based on the increased bioavailability of NADH and an increase of the ATP level in the cell by an average by 7%. The consequences of the lower lactate levels in the blood after regular intake of NADH is that athletes can exercise longer under aerobic conditions, and in turn this improves their endurance performance.

NADH improves cognitive performance

The effect of NADH on cognitive performance (reduced by sleep deprivation) was investigated at the Department of Sleep medicine at Cornell University in New York. Healthy individuals, 30 to 45 years of age, were kept awake for 24 hours under EEG control. 24 hours of sleep deprivation causes a decrease in attention, capability to concentrate, slowing of reaction time and visual perception as well as the skill of solving mathematical problems. Subjects taking 20 mg of NADH did not only

better in terms of cognitive performance than the placebo subjects but did more than 3 times better than the same subjects at base line, after a full night sleep (11). In other words, NADH enhances cognitive performance in healthy individuals. This energy-increasing effect of NADH on the brain could prevent MCI (Mild Cognitive Impairment), as well as Alzheimer dementia.

NADH and its oxidized form, NAD^+ , mediate numerous major biological processes, including calcium homeostasis, energy metabolism, mitochondrial functions, cell death and aging. (12). These coenzymes have emerged as fundamental regulators of calcium homeostasis. It appears that most of the components in the metabolic pathways of NAD^+ and NADH, including poly (ADP-ribose) and ADP-ribose can produce significant biological effects. (13) NADH, together with ATP and Ca^{2+} , constitute a Central Regulatory Network of life. NADH may also prevent brain aging and tissue damage in various brain illnesses. NADH can be transported across the plasma membranes of astrocytes, and due to this it can markedly decrease ischemic brain injury.

NADH in learning and memory

An ADP-ribosyl transferase (ART) activity was found in the hippocampal CA1 tissues, which was dramatically stimulated by NO and attenuated by two different inhibitors of ARTs (14). ART inhibitors were found to block long-term potentiation --- an important process in learning and memory. These results suggest that the NAD^+ -dependent ARTs may play a significant role in long-term potentiation. Ca^{2+} released from presynaptic and postsynaptic intracellular stores plays important roles in activity-dependent synaptic plasticity, including long-term depression of synaptic strength. Due to the critical roles of Ca^{2+} homeostasis, energy metabolism and gene expression in learning and memory, NADH and NAD^+ may further affect cognitive functions by influencing these important biological properties.

Roles of NADH and NAD^+ in the gene expression of brains

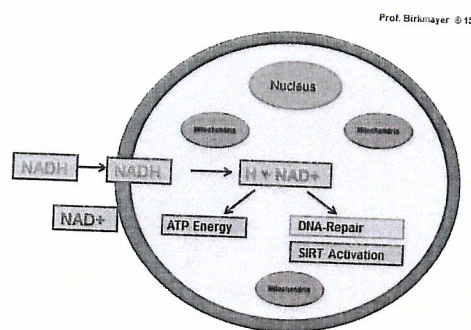
NADH and NAD^+ may affect gene expression through multiple-mechanisms : First, sirtuins can affect gene expression by several pathways : Yeast Sir2 can silence gene transcription (15); sirtuins can also mediate the activities of the transcriptional factors such as p53. Second, PARP-1 can affect several transcriptional factors such as p53, AP-1 and NF- κ B. Third, NAD^+ is required for the activities of other PARPs such as tankyrases, which could also affect gene expression (16). Fourth, NADH regulates the activity of the corepressor carboxyl-terminal binding protein --- a transcriptional factor for development, cell cycle regulation and transformation (17) ; and NADH

also regulates Clock: BMAL1 and NPAS2:BMAL1 - the heterodimeric transcription factors modulating the gene expression in the circadian clock (18). However, it has to be pointed out that NAD⁺, as charged molecule, does not penetrate the cell membrane (1). However, NADH is transported through the cell membrane into the cell, where it is oxidized to NAD⁺ and the hydrogen. The latter is then converted to water and ATP energy (see figure 1).

NADH and NAD⁺ in aging

Repeated administration of NADH was found to improve the performance of old rats in the Morris water maze studies, suggesting the capacity of NADH to enhance the cognitive functions of old rats (19). Old cells age us. Inside a cell, telomeres at the end of each chromosome contain genetic information that gets clipped away with each cell division. At first, telomeres are long enough that they can handle a snip here and a trim there. But after they hit a certain length, the information is lost. For John Harris, a bioethicist at the University of Manchester, England, emphasizes that scientists have a moral duty to extend the human life span as far as it will go, made clear when he said ; "When you save a life, you are simply postponing death to another point, thus, we are committed to extending life indefinitely if we can, for the same reasons that we are committed to life-saving." A number of scientists say we may be close to achieving lifetimes that are at least several decades longer. The realization of this dream will come from a scientific understanding of how aging affects our bodies at the cellular and molecular levels. Scientists go back and forth on the feasibility of slowing, halting or even reversing the aging process. Researchers would very much like to develop a pill that let us live twice as long while remaining free of infirmities. NADH in its stabilized form developed by the author and available as a nutritional supplement, appears to fulfill this wish for longevity. Dr. Richard A. Passwater, a biochemist and expert in antioxidants writes in his foreword of the book 'NADH - The Energizing Coenzyme' "While there is no such thing as a singular 'most important' antioxidant in the body NADH comes as close as a single compound can." (20)

Figure 1 : NADH uptake into a cell



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