LIDTKE
TECHNOLOGIES

Purest on the Planet... *Since 1994*

Understanding NAD:

the Assimilation of Precursors, its Generation in vivo, and its Effects on Aging and Human Health

Currently, the lead scientist in NMN research at the Harvard Medical school, David A. Sinclair, Ph.D., A.O., (now a little over 50 years of age) takes 1 gram of NMN per day. Based on the research at Harvard, he has concluded that NMN (short for beta-nicotinamide mononucleotide) is the best way to increase NAD+ (Nicotinamide adenine dinucleotide) levels in the human body.

NAD is found in all living cells. It makes redox reactions possible by carrying electrons from one reaction to another. NAD+ takes electrons from other molecules and becomes NADH. NADH donates electrons. This is an important process that makes life possible.

As a result, NAD+ is involved in many important health processes. A decline in NAD+ levels is responsible for aging-related decline and the dysregulation of many biological functions. Of particular note, NAD+ plays a vital role in mitochondrial function, needed in the generation of ATP, the body's energy system.[1,2]

Studies have shown that NAD+ also plays a critical role in DNA repair,[3] the metabolism of food,[4] new blood vessel formation,[5,6] the circadian cycle,[7,8] and much more.

NAD+ is constantly recycled by the body, but there are some processes for which it cannot be recovered; hence your body does have an absolute need to consume more NAD building blocks. At the same time, nutrients that slow the body's loss of NAD+ might also be deemed critical.

As humans age, their NAD+ levels decline, at the same time as their need increases. Studies have shown that NAD+ is destroyed by enzyme CD38 and that levels of this destructive enzyme increase with age.[9] As CD38 increases with age, then, NAD+ predictably decreases. Although it is not fully understood how or why the body increases CD38 levels, it is important to note that NAD+ is a victim.

Tests have shown that mice bred to be deficient in CD38 enjoy increased

protection from mitochondrial dysfunction and are resistant to diabetes as they age. This protective action is regulated via the mitochondrial sirtuin SIRT3. Predictably, research shows that mice treated with a CD38 inhibitor have increased levels of NAD+.[10]

With all the important discoveries surrounding NAD+ and the clear benefits of increasing NAD+ levels, it is clear why scientists are ramping up human clinical studies.

The Rise of NMN

In hindsight, a number of assumptions were made early-on that turned out to be false. Researchers now know that NMN does enter a cell directly, and in fact it has a specific transporter called Slc12a8.[15] In mice (and it is thought humans too), Slc12a8 expression is roughly 100 times higher in the small intestine than in brain or fat tissue.

This is consistent with the evidence from mice that NMN dramatically improves their physiological function. In these studies NMN is added to their *drinking water*; it is not injected into the bloodstream or placed under their tongues to be absorbed.

You may be familiar with the fact that 90 percent of the body's serotonin is made in the digestive tract. Digestion is after all the body's primary way of taking in nutrients, so it should not be a surprise that many of the body's most important biological processes are rooted in the gut. The lesson learned here is that NAD+ generation from the ingestion of NMN appears to work perfectly well passing through the gut.

The first human clinical trials of NMN have already been completed.[19] One of the scientists involved, Shin-ichiro Imai, spoke with reporters, affirming the many promising observation, including the faster absorption of NMN. In addition, basic safety has been established in humans, although this was fully expected due to the results with mice. More human clinical trials are already being planned.

References

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4487780/

[2] https://www.khanacademy.org/testprep/mcat/biomolecules/krebs-citric-acid-cycle-and-oxidativephosphorylation/a/oxidative-phosphorylation-the-majorenergy-provider-of-the-cell

[3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5384578/

[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5668137/

[5] https://hms.harvard.edu/news/rewinding-clock

[6] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6477631/

[7] "The Time of Metabolism: NAD+, SIRT1, and the Circadian Clock" http://symposium.cshlp.org/content/76/31.full.pdf

[8] https://www.hindawi.com/journals/bmri/2016/3208429/

[9] NAD declines with age https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4911708/

[10] Escande, C., Nin, V., Price, N. L., Capellini, V., Gomes, A. P., Barbosa, M. T., … & Chini, E. N. (2013). Flavonoid apigenin is an inhibitor of the NAD+ ase CD38: implications for cellular NAD+ metabolism, protein acetylation, and treatment of metabolic syndrome. Diabetes, 62(4), 1084-1093.

[11] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5842119/

[12] Review of various NAD+ precursors https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6359187/

[13] https://jbiomedsci.biomedcentral.com/articles/10.1186/s12929-019-0527-8

[14] Examples can be provided

[15] https://www.researchgate.net/publication/330203173_The_elusive_NMN_transporter_is_found

[16] https://www.cell.com/cell-metabolism/fulltext/S1550-4131(18)30196-7

[17] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4646395/

[18] NAM and neurons https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2677622/

[19] Human trial NMN https://www.jstage.jst.go.jp/article/endocrj/advpub/0/advpub_EJ19-0313/_article