ETHIOPIAN INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 11, Issue 02, Fev-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980

# METOBOLISM OF NICOTINAMIDE ADENINE DINUCLEOTIDE

**Qosimov Abduqodir**

Andijan State Medical Institute

**Annotation:**In this article you will get interesting and important information about the synthesis of nicotinamide adenine dinucleotide (NAD+). Nicotinamide adenine dinucleotide (NAD+) is an important pyridine nucleotide and serves as an important cofactor and Substrate for a number of important cellular processes related to oxidative phosphorylation and ATP production, DNA repair, epigenetically modulated gene expression, intracellular calcium signaling, and immunological functions. This article was written on the internet networks, in the case when the scientific work of various scientists was used.

**Key words:**Nicotinamide adenine dinucleotide, ATP, NAD, DNA, RNA.

Nicotinamide adenine dinucleotide (NAD) is a coenzyme central to metabolism.] Found in all living cells, NAD is called a dinucleotide because it consists of two nucleotides joined through their phosphate groups. One nucleotide contains an adenine nucleobase and the other, nicotinamide. NAD exists in two forms: an oxidized and reduced form, abbreviated as $NAD^+$ and NADH (H for hydrogen), respectively.

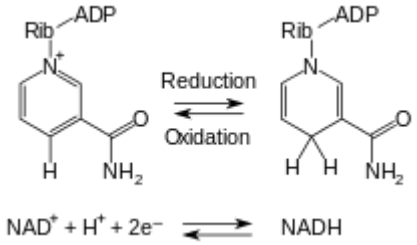
In cellular metabolism, NAD is involved in redox reactions, carrying electrons from one reaction to another, so it is found in two forms: $NAD^+$ is an oxidizing agent, accepting electrons from other molecules and becoming reduced; with $H^+$, this reaction forms NADH, which can be used as a reducing agent to donate electrons. These electron transfer reactions are the main function of NAD. It is also used in other cellular processes, most notably as a substrate of enzymes in adding or removing chemical groups to or from proteins, in posttranslational modifications. Because of the importance of these functions, the enzymes involved in NAD metabolism are targets for drug discovery.

In organisms, NAD can be synthesized from simple building-blocks (de novo) from either tryptophan or aspartic acid, each a case of an amino acid. Alternatively, more complex components of the coenzymes are taken up from nutritive compounds such as niacin; similar compounds are produced by reactions that break down the structure of NAD, providing a salvage pathway that recycles them back into their respective active form.

Some NAD is converted into the coenzyme nicotinamide adenine dinucleotide phosphate (NADP), whose chemistry largely parallels that of NAD, though its predominant role is as a coenzyme in anabolic metabolism.

In the name $NAD^+$, the superscripted plus sign indicates the positive formal charge on one of its nitrogen atoms.

eISSN: 2349-5715 pISSN: 2349-5707
Volume: 11, Issue 02, Fev-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980




PELLAGRA IS A SYNDROME cause by a diet seriously deficient in synthetic precursors for the essential pyridine nucleotide nicotinamide adenine dinucleotide ($NAD^+$), namely niacin (vitamin B3), and tryptophan . This lethal disorder can develop within 60 days of maintaining a deficient diet due to the absence of free stores of nicotinic acid (NA) or nicotinamide (NAM) . Pellagra is pathologically characterized by a distinct dark pigmented skin rash and the three Ds of dermatitis, diarrhea, and dementia . Interestingly, the AIDS dementia complex (ADC) shares some neurological similarities with pellagra in its clinical presentation .

In the last century, pellagra was a common disease in rural areas in the poorer southern United States, and was attributed to an unknown infectious pathogen . However, it was Dr. Joseph Goldberger, and his associates, of the U.S. Public Health Service, who in 1914 examined the hypothesis that pellagra was due to a dietary deficiency. Subsequently, pellagra was prevented using a diet rich in maize, fresh milk, eggs, and cured meat in these populations . Despite these advances, it was not until 1937 that Conrad Elvehjem, a biochemistry Professor, first demonstrated the anti-pellagra genic effect of NAM and NA on the related black tongue disease in malnourished dogs [1].

Several biochemical studies have shown that an inefficient production of $NAD^+$, where catabolism exceeds anabolism, may produce cellular dysfunction simply due to dietary lack of niacin . It may also be due to the rate-limiting action of cosubstrate-dependent quinolinic acid phosphoribosyltransferase (QPRT) . Excess amino acid leucine inhibits QPRT, which prevents the formation of niacin or NA to nicotinic acid mononucleotide (NAMN) . Reduced tryptophan availability, particularly after chronic immune activation or in the absence of a tryptophan-rich diet (i.e., soy, meat, fish, eggs, and peanuts), may also be associated with the development of pellagra. Essential differences, however, may be observed between ADC and pellagra, as the latter develops as a result of a global bodily deficiency of tryptophan and niacin, while ADC develops as a result of increased tryptophan and $NAD^+$ catabolism at specific, although possibly numerous, sites . Activation of the tryptophan catabolism may be both positive and negative in ADC. Immune-activated oxidative tryptophan catabolism can positively increase cell viability through increased $NAD^+$ metabolism in brain cells. However, chronic activation of tryptophan catabolism may occur in response to increased $NAD^+$ catabolism. Increased astrocyte and mononuclear phagocyte activation stimulates tryptophan catabolism to maintain $NAD^+$ levels in the early stages of immune activation. However, prolonged immune activation leads to excess macrophage recruitment and activation,

[1] Public Health Reports, June 26, 1914. The etiology of pellagra. The significance of certain epidemiological observations with respect thereto. *Public Health Rep* 90: 373–375, 1975 [PMC free article] [PubMed] [Google Scholar] [Ref list]

eISSN: 2349-5715 pISSN: 2349-5707
Volume: 11, Issue 02, Fev-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980

reducing the astrocyte-to-neuronal $NAD^+$ supply, resulting in pellagra-like neuronal dysfunction, which may be reversible in the short term.

It is well known that $NAD^+$ concentrations increase under conditions associated with reduced energy loads. These include activities such as fasting, glucose deprivation, caloric restriction (CR), and exercise . However, apart from pellagra, $NAD^+$ levels decline in animals on high-fat diets, and during aging and cellular senescence. Given that $NAD^+$ levels are elevated under conditions of increased life span or health span, decline under conditions of accelerated aging and/or reduced health span suggests that reduced $NAD^+$ levels may represent a major contributor to the aging process. Therefore, supplementation with $NAD^+$ and its precursors may represent a potential therapeutic strategy to mediate protection against accumulation of inflammation and highly volatile reactive oxygen species (ROS) during the aging process.[2]

Cigarettes are designed to efficiently deliver nicotine to the user. Therefore, nicotine itself or its metabolites are arguably the most reliable biomarkers for smoking exposure. Nicotine has a relatively short half-life (1–2 h). Whereas, cotinine has a half-life of 8 to 30 h, and the presence of cotinine in either blood or urine is widely used as a biomarker of tobacco exposure . Cotinine is the most abundant nicotine metabolite present in blood but typically accounts for <15% of the nicotine dose excreted in urine. The most commonly used urinary biomarker of tobacco exposure is total nicotine equivalents, which is the sum of the molar concentrations of nicotine and six metabolites.
Both blood and urine cotinine concentrations are affected by individual differences in nicotine and cotinine metabolism. One smoker who metabolizes either compound more or less efficiently than another smoker will likely have different levels of cotinine for the same nicotine dose. This is particularly important in the study of racial/ethnic differences in tobacco-related disease risk, since the frequencies of UGT2B10 and CYP2A6 alleles vary by racial/ethnic group. In addition, it has been recognized for many years that African Americans, who are active smokers or who are exposed to secondhand tobacco smoke, have significantly higher cotinine concentrations than whites with similar exposure .
With the exception of smokers who carry two CYP2A6 deleted alleles, UGT2B10 variants and cotinine glucuronidation levels influence blood cotinine concentrations significantly more than does P450 2A6 activity. At similar levels of smoking, individuals who are homozygous for the CYP2A6* 4 deletion allele have significantly lower plasma cotinine levels than do individuals who carry CYP2A6 alleles coding for fully functional enzymes. However, in smokers with reduced P450 2A6 activity, the relationship of enzyme activity to plasma cotinine levels is complicated since both the formation of cotinine and its further metabolism is mediated by P450 2A6. Cotinine clearance, not formation, appears to dominate this process since plasma cotinine concentrations tend to be higher in individuals with detectable but reduced P450 2A6 activity . A significant amount of cotinine is metabolized by UGT2B10-catalyzed glucuronidation, and total cotinine clearance is 50% lower in individuals who are homozygous for the UGT2B10 splice variant compared with those who do not carry this allele. The decreased clearance of cotinine in these smokers results in 45% higher serum cotinine levels (genetic score 0 versus 2). Smokers who are heterozygous for either the

[2] Scheibye-Knudsen M, Mitchell SJ, Fang EF, Iyama T, Ward T, Wang J, Dunn CA, Singh N, Veith S, Hasan-Olive MM, Mangerich A, Wilson MA, Mattson MP, Bergersen LH, Cogger VC, Warren A, Le Couteur DG, Moaddel R, Wilson DM, 3rd, Croteau DL, de Cabo R, and Bohr VA. A high-fat diet and NAD(+) activate Sirt1 to rescue premature aging in cockayne syndrome. *Cell Metab* 20: 840–855, 2014 [PMC free article] [PubMed] [Google Scholar] [Ref list]

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 11, Issue 02, Fev-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980

UGT2B10 splice variant or the Asp67Tryr variant have on average 19% higher plasma cotinine concentrations. These differences are observed after adjustment for smoking dose (cigarettes per day and total nicotine equivalents) and P450 2A6 activity.

**References**

1. Dalimova, M. (2023). ORIGIN AND PATHOGENESIS OF THE CURRENTLY COMMON ALBINISM DISEASE. Ethiopian International Journal of Multidisciplinary Research, 10(09), 378-383.
2. Dalimova, M. (2023). The Importance of The Process of Metabolism on The Body. Central Asian Journal of Medical and Natural Science, 4(6), 373-377.
3. Mukhtorovna, D. M. (2022). Digestive system activity in people of different ages. Texas Journal of Medical Science, 12, 68-71.
4. Mukhtarovna, D. M. (2022). THE ORIGIN OF MIASTHENIA DISEASE AND METHODS USED IN TREATMENT. American Journal of Interdisciplinary Research and Development, 10, 258-261.
5. Nurumbetova, S. (2022). VAIN ASPECTS OF PRACTICAL RELIGIOUS EXAMINATION IN THE INVESTIGATION OF CRIMES RELATED TO PROHIBITED RELIGIOUS MATERIALS. Science and Innovation, 1(6), 108-113.
6. Nurumbetova, S. (2023). MODERN OPPORTUNITIES AND PROSPECTS FOR DEVELOPMENT EXPERT-CRIMINALISTIC ACTIVITY. Modern Science and Research, 2(9), 415-419.
7. Нурумбетова, С. А. (2023). СОВРЕМЕННЫЕ ВОЗМОЖНОСТИ И ПЕРСПЕКТИВЫ РАЗВИТИЯ ЭКСПЕРТНО-КРИМИНАЛИСТИЧЕСКОЙ ДЕЯТЕЛЬНОСТИ.
8. Мухамедова, М. Г., Куртиева, Ш. А., & Назарова, Ж. А. (2020). СИНДРОМ ФУНКЦИОНАЛЬНОЙ КАРДИОПАТИИ У СОВРЕМЕННЫХ ПОДРОСТКОВ. In П84 Профилактическая медицина-2020: сборник научных трудов Все-российской научно-практической конференции с международным участи-ем. 18–19 ноября 2020 года/под ред. АВ Мельцера, ИШ Якубовой. Ч. 2.—СПб.: Изд-во СЗГМУ им. ИИ Мечникова, 2020.—304 с. (p. 105).
9. Kurtieva, S., Nazarova, J., & Mullajonov, H. (2021). Features of endocrine and immune status in adolescents with vegetative dystonia syndrome. International Journal of Health Sciences, 5(2), 118-127.
10. Kurtieva, S., Nazarova, J., & Mullajonov, H. (2021). Features of Physical and Generative Development of Modern Teenagers Living in Uzbekistan. NeuroQuantology, 19(7), 57.
11. Куртиева, Ш. (2021). CHANGES IN ELECTROENCEPHALOGRAM INDICATORS IN ADOLESCENTS WITH VEGETATIVE DYSFUNCTION. УЗБЕКСКИЙ МЕДИЦИНСКИЙ ЖУРНАЛ, (SPECIAL 3).
12. Kurtieva, S. (2022). INDICATORS OF THE EXTERNAL RESPIRATORY SYSTEM AND CARDIAC ACTIVITY IN ADOLESCENTS. Frontline Medical Sciences and Pharmaceutical Journal, 2(01), 17-24.
13. Kurtieva, S. (2021). Physical Performance Assessment in Adolescents with Autonomic Dysfunction. International Journal Of Medical Science And Clinical Research Studies, 1(6), 143-146.