



Description

Acetaldehyde, glycolysis, TCA cycle flux and other mitochondrial matrix NADH generators (not shown - see Figure 17) decrease the mitochondrial NAD⁺ pool and increase NADH pool sizes.

Complex I (NADH Dehydrogenase) normally balances this NAD⁺:NADH redox, however is inhibited by reactive oxygen and nitrogen species, primarily generated by uncoupled NOS and NOX activity - promoted by interferon signalling cascades and acetaldehyde directly.

Where Complex I is inhibited, GDH and NADPT activity is increased by the NADH pool elevation, further increasing glutamate and the NADPH pool, promoting regulatory glutathione peroxidase and other synthesis activities.

Methylene blue concentrates in the mitochondrial matrix, providing a narrow therapeutic window for creating a parallel electron pathway to Cytochrome c and NAD⁺ redox support.

- Ag - Silver
- α-KGDH - Alpha-Ketoglutarate Dehydrogenase
- ALDH - Aldehyde Dehydrogenase
- ADP - Adenosine Diphosphate
- ATP - Adenosine Triphosphate
- Au - Gold
- cAMP-PKA - Cyclic Adenosine Monophosphate - Protein Kinase A
- Cd - Cadmium
- CD38 - Cluster of Differentiation 38 (NAD⁺ glycohydrolase)
- COMPLEX I - NADH:Ubiquinone Oxidoreductase
- DOPAL - 3,4-Dihydroxyphenylacetaldehyde
- eATP - Extracellular Adenosine Triphosphate
- FAD - Flavin Adenine Dinucleotide
- GCL - Glutamate-Cysteine Ligase
- GLS - Glutathione Synthase
- GPx - Glutathione Peroxidase
- GR - Glutathione Reductase
- GDH - Glutamate Dehydrogenase
- GHB - gamma-Hydroxybutyrate
- H₂O - Water
- H₂O₂ - Hydrogen Peroxide
- Hg - Lead
- IDH - Isocitrate Dehydrogenase
- IFN - Interferon
- LPA - Lipoamide
- MB⁺ - Methylene Blue
- MBH₂ - Leucomethylene Blue
- MDH - Malate Dehydrogenase
- Mo²⁺ - Molybdenum Ion
- Mg²⁺ - Magnesium Ion
- NAD⁺ - Nicotinamide Adenine Dinucleotide (oxidised)
- NADH - Nicotinamide Adenine Dinucleotide (reduced)
- NADP - Nicotinamide Adenine Dinucleotide Phosphate (oxidised)
- NADPH - Nicotinamide Adenine Dinucleotide Phosphate (reduced)
- NADPT - NAD(P) Transhydrogenase
- NMNAT - Nicotinamide Mononucleotide Adenylyltransferase
- NOS - Nitric Oxide Synthase
- NOX - NADPH Oxidase
- OxPPP - Oxidative Pentose Phosphate Pathway
- Pb - Lead
- P5P - Pyridoxal 5-Phosphate
- PDH - Pyruvate Dehydrogenase
- Pi - Inorganic Phosphate
- PRPP - 5-Phosphoribosyl-1-Pyrophosphate
- Q - Ubiquinone
- QH₂ - Ubiquinol
- ROS - Reactive Oxygen Species
- RNS - Reactive Nitrogen Species
- TCA - Tricaric Acid
- THP - Tetrahydropapaveroline
- TPP - Thiamine Pyrophosphate
- Zn²⁺ - Zinc Ion

Figure 14. Pathway Diagram: A simplified overview of mitochondrial NAD⁺:NADH deficiency.
ME/CFS: Correcting Chronic Mitochondrial Dysfunction
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