

NAD's dinucleotide structure enables specific reduction on mineral surfaces

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Nucleotide-derived cofactors are small molecules, essential to metabolism that could be a missing link between the informational and the metabolic part at life's emergence. A well-known example is nicotinamide dinucleotide (NAD), one of the evolutionarily most conserved redox cofactors found in metabolism. We propose that these cofactors have functioned as important missing links between geo- and biochemistry. Before modern-like proteins emerged, small cofactors would have sufficed to establish pathways between different environments and immobile catalysts such as minerals, through biomolecule-mineral interactions. We first show how NAD⁺ can be reduced specifically to the biologically relevant form of NADH under close-to nature conditions with nickel-iron-alloys found in water-rock-interaction settings rich in hydrogen (serpentinizing systems). Nicotinamide mononucleotide (NMN), a precursor molecule to NAD lacking the adenosine monophosphate (AMP) part of the dinucleotide, gets reduced far less specifically, leading to a variety of reduction side products. When reduced in direct competition, the concentration of 1,4-NADH always surpasses that of NMNH. The reduction specificity of NMN also depends on the type of transition metal present, which leads to the conclusion that the environment could have had an important influence on a prebiotic, pre-enzymatic selection of cofactors. NMNH side products were shown to have less reducing strength than NMNH under abiotic conditions, while NADH is an equally effective soluble hydride donor. The differences observed between NAD(H) and NMN(H) revealed that the AMP "tail" of the dinucleotide, a shared trait between many organic cofactors, seems to be necessary to prevent overreduction of the nicotinamide-bearing nucleotide in our mineral-based setup, and attributes a competitive advantage when both molecules are present.