Prebiotic Formation of Protoalkaloids within Alkaline Oceanic Hydrothermal Vents in the Hadean Seafloor as a Prerequisite for Evolutionary Biodiversity

George B. Stefano
Richard M. Kream

Corresponding Author: George B. Stefano, e-mail: gstefano@sunynri.org

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The primordial origin of abiotic nitrogen fixation, which is not dependent on prokaryotes, reflects the importance of available nitrogenous compounds as an essential requirement for the emergence of life and evolutionary biodiversity. It has been hypothesized that synthesis of oxidized nitrogen in the form of nitrate (NO$_3^-$) and nitrite (NO$_2^-$), occurred in the prebiotic anoxic Hadean atmosphere. The sustained influx of atmospheric NO$_3^-$ and NO$_2^-$ into prebiotic Hadean oceans have been proposed to provide the essential substrates for abiotic synthesis of compounds such as ammonia (NH$_3$) within oceanic alkaline hydrothermal vents in the seafloor. Because NH$_3$ is an essential chemical precursor for nitrogen-containing molecular components of proteins and nucleic acids, abiotic production in high concentrations within Hadean oceanic alkaline hydrothermal vents is required for the emergence of diverse life forms. The chemical evolution of nitrogenous compounds includes the functional development of alkaloids. This commentary aims to critically discuss the possible origin of nitrogen-containing alkaloids and evolutionary processes in higher organisms, including the diverse biomedical mechanisms involved.

MeSH Keywords: Alkaloids • Evolution, Molecular • Hydrothermal Vents • Morphine • Nitric Oxide • Nucleic Acids

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Nitrogen is assumed to be a relatively inert gaseous element that represents approximately 78% of the earth’s atmosphere. The assumed relative stability of nitrogen as the major component of the atmosphere can obscure the existential importance of nitrogen fixation and recycling within the biosphere. The primordial origin of nitrogen fixation and chemical diversity reflects the importance of bioavailable reservoirs of nitrogenous compounds as essential requirements for the emergence of life on earth. Theories of the origins of life have focused on the critical role of alkaline hydrothermal vents in the ocean floor during the anoxic Hadean period, approximately 4.2 billion years ago [1,2]. These alkaline hydrothermal vents function as electrochemical flow reactors utilizing iron and nickel mineral surfaces that contain sulfides to catalyze the reduction of CO2 by H2 to eventually form methane [1,2]. Also, the synthesis of chemical species of oxidized nitrogen in the prebiotic anoxic Hadean atmosphere may have been initiated prebiotically by nitric oxide (NO) formation from N2 and CO2 by lightning discharges, followed by photochemical production of nitrate (NO3-) and nitrite (NO2-) anions from NO and H2O vapor [3]. During millions of years, sustained fluxes of atmospheric NO3- and nitrite NO2- into prebiotic Hadean oceans have been proposed to provide the essential substrates for abiogenic NH3 synthesis in alkaline hydrothermal vents in the ocean floor [4]. Because NH3 is an essential chemical precursor for nitrogen-containing molecular components of proteins and nucleic acids, amino acids, purine and pyrimidine bases, the abiotic production of high concentrations of NH3 in the ocean represents an essential requirement for the emergence of diverse life forms in the Archean Eon, which occurred 4,000 to 2,500 million years ago.

In 2018, Russell proposed that the sediments surrounding alkaline hydrothermal vents consisted of micro or nanocrystals of Fe (II)-Fe (III) oxyhydroxide known as ‘green rust’ [5]. The combination of ‘green rust’ with iron sulfides and small concentrations of nickel, cobalt, and molybdenum, might have been the required chemical catalysts to expand the chemical diversity required for the emergence of life [5]. Russell also proposed that ‘green rust’, combined with sulfides and trace elements, facilitated abiotic synthesis of acetate and higher carboxylic acids leading to the formation of alpha-amino acids following chemical amination [5]. In 2009, Garvin et al. reported the findings from an empirical geochemical study of marine sediment [6]. The findings suggested that nitrifying and denitrifying microbes had already evolved by the late Archean Eon, approximately 2.5 billion years ago, before the accumulation of atmospheric O2, and in response to small increases in ocean oxygenation [6]. Therefore, it is possible to conclude that parallel and potentially synergistic abiotic and microbial chemical synthetic processes promoted the exponential expansion of nitrogen-containing organic compounds before significant atmospheric O2 accumulation and in anticipation of the metabolic demands of a photosynthetic-dependent biosphere.

The chemical evolution of nitrogenous compounds has focused on the functional elaboration of alkaloids, including primary amines composed of simple straight-chained structures, such as amino acids, or internally bonded secondary and tertiary amines within more complex heterocyclic structures. Morphine represents a relatively low molecular weight heterocyclic alkaloid that has been evolutionarily fashioned from an alkaloid with a relatively restricted role [1,2,7]. Morphine ‘evolved’ from a secreted antimicrobial phytoalexin into a broad spectrum endogenous regulatory molecule mediating diverse physiological responses in animal cellular systems [1,2,7]. Furthermore, in the prebiotic time period, the alkaline hydrothermal vents in the ocean floor also provided an energy-generating iron-dependent system for chemical energy utilization and production across the primitive cell membrane, which involved nitrogenous chemical species, such as alkaloids and adenosine triphosphate (ATP) [1,2,7].

Therefore, the predominance of nitrate, nitrite, and NO and as oxidizing substrates within the prokaryotic nitrogen cycle might have been most likely to have facilitated the evolutionary development of eukaryotic enzyme-mediated aerobic respiration requiring O2 reduction by heme-copper oxygen reductases (HCOs) as the terminal enzymatic step [7]. Interestingly, the aerobic respiratory system is found in mitochondria, which originated from prokaryotic cells, revealing an unmistakable evolutionary fingerprint. Therefore, it would appear that prebiotic alkaline hydrothermal vents in the ocean floor provided an evolutionarily conserved common molecular theme of nitrogen-derived chemicals. These nitrogen-derived chemicals were then maintained in an intracellular environment used for information transfer, energy-associated processes, and intracellular and intercellular signaling. This hypothesis is supported by the link between endogenous morphine with energy metabolism and cellular signaling, including direct and indirect actions on DNA [8–10]. A further common association between these alkaloid-associated functions, which are important for all life forms, is the morphine alkaloid is coupled to constitutive NO release, and may act as a ‘second messenger’ resulting in the final effects [7,11]. Therefore, alkaloids have been constitutively retained during evolution.

Conclusions

The chemical structure of alkaloids are extremely variable but are critical in evolution and evolutionary biodiversity.
The evolution of alkaloids may have been made possible due to their association with the cell membrane and their association with early energy processes. The function and significance of alkaloids have been enhanced during evolution, particularly by their critical presence in genetic, structural, and molecular signaling mechanisms. Endogenous morphine, as a representative molecule, has an influence on several life-sustaining processes in addition to its effects on pain perception. However, the significance of alkaloids and their evolutionary biodiversity roles have received little attention, possibly due to lack of research and a lack of understanding of their importance. Also, morphine may not be recognized as an alkaloid. It is hoped that this brief update on the prebiotic formation of protoalkaloids within alkaline oceanic hydrothermal vents in the Hadean seafloor and evolutionary biodiversity has highlighted their significance, and that novel therapeutic agents may be developed for associated clinical disorders such as the management of opiate abuse.

**Conflict of interest**

None.

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