July 16-21, 2017 at UC San Diego, CA, USA

An Evaluation of the Prebiotic Plausibility of Depsipeptide Synthesis Under Possible Primitive Conditions

E. T. Parker[1,2], J. G. Forsythe[1,3] and F. M. Fernández[1,*],
[1]Georgia Institute of Technology, Atlanta, GA; [2]Present Institution: NASA Goddard Space Flight Center, Greenbelt, MD; [3]Present Institution: College of Charleston, Charleston, SC
* facundo.fernandez@chemistry.gatech.edu

Introduction: Although numerous reports exist demonstrating the prebiotic synthesis of organic monomers [1-3], the polymerization of such species on the early Earth to form biopolymers important for life remains poorly understood. Recently, the plausible prebiotic condensing reagent cyanamide was shown to polymerize amino acids to generate simple peptides under mimicked primordial conditions [4], but the formation of diketopiperazines, cyclic dipeptides that can limit the availability of amino acid residues for further polymerization chemistry, remained a challenge. More recently, simulated dry-hot/wet-cool environmental cycling has demonstrated the ability to co-polymerize amino acids and alpha-hydroxy acids to generate depsipeptides (containing mixed amide/ester linkages), becoming enriched in amide linkages over time [5], supporting the hypothesis that peptides may have evolved from ester-based precursors. However, these results were obtained using neat standard solutions of a limited number of monomers present at relatively high concentrations. Analyses of primitive simulation experiments suggest prebiotic mixtures are far more complex and produce relatively small quantities of relevant monomers [6]. Ideally, a more robust evaluation of the prebiotic plausibility of depsipeptide synthesis would be executed, entailing the performing of primordial simulation experiments and subjecting the resultant mixtures to mimicked environmental cycling, prior to analysis for depsipeptides.

Methods: Here, we report the development of the first multi-stage analytical platform for the analysis of didepsipeptides in complex mixtures, using ultra performance liquid chromatography, traveling wave ion mobility spectrometry, and high resolution tandem mass spectrometry. Additionally, prebiotic experiments were performed and their resultant solutions were subjected to simulated environmental cycling to constrain the viability that the amino acids and alpha-hydroxy acids formed in-situ could have co-polymerized to yield didepsipeptides.

Results: The results of this investigation provide the first detection of depsipeptides in complex, prebiotic mixtures. Example depsipeptides detected included the glycolic acid-aspartic acid and malic acid-glycine didepsipeptides. Detection of didepsipeptides was further elucidated via acid hydrolysis-, internal standard spiking-, and isotopic labeling experiments.

Implications: The overarching implication of this work is that it provides new insight into the chemical evolution processes that may have been responsible for the synthesis of prebiotic peptides under a variety of possible primordial environments.

References:

[1] Miller SL (1953) *Science* 117:528–529. [2] Johnson AP et al. (2008) *Science* 322:404. [3] Parker ET et al. (2011) *Proceedings of the National Academy of Sciences U.S.A.* 108:5526–5531. [4] Parker ET et al. (2014) *Angewandte Chemie, International Edition* 53:8132–8136. [5] Forsythe JG et al. (2015) *Angewandte Chemie, International Edition* 54:9871–9875. [6] Parker ET et al. (2016) *Rapid Communications in Mass Spectrometry* 30:2043–2051.