Amplification of Chirality via the Amyloid-Based Aggregation of Isotactic Peptides.

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Of the many known abiotic sources of molecular asymmetry, those that are relevant to the origin of life produce an enantiomeric excess (ee) of only few percent. Therefore a relevant yet unanswered question is: can a small ee be amplified to homochirality under prebiotic conditions? To date there have been several reports of chiral amplification based on the stereoselective effects of amino acid N-carboxyanhydride (NCA) polymerization [1, 2] and polypeptide aggregation [3, 4]. In organic solvents it has long been observed that the polymerization of the NCAs of amino acids can be stereoselective, that is the chirality of the growing peptide will dictate a preference for condensation with one of the enantiomers of the NCA [1, 5]. This stereoselective effect is also present in aqueous polymerizations of the NCAs of some amino acids [6, 7]. More recently it has been discovered that there is a strong tendency for the aqueous polymerization of racemic hydrophobic amino acids to yield precipitates that are highly enriched for isotactic sequences [8]. The underlying mechanism, while still open to investigation almost certainly involves the formation of racemic (so-called rippled) beta sheet aggregates. This interesting effect, while providing a source of long homochiral peptides, cannot account for the chiral amplification of L or D amino acids. Despite these interesting effects of amino acid polymerization and isotactic peptide precipitation, there is no inherent chiral resolution, or separation of the L and D isomers. Therefore, other mechanisms are required to amplify a pre-existing ee of amino acids via these processes.

The statistical variation in a binomial distribution offers one possibility: concerning the isotactic peptides that result from the polymerization of a scalemic amino acid mixture, the longer the isotactic polymer is, the higher will be its ee, but with lower overall yield (described in [9]). In the absence of stereoselectivity, the ee of a monomer given as $\mathrm{ee}_{monomer} = \frac{\chi_L - \chi_D}{\chi_L + \chi_D}$ will result in a final ee of isotactic n-mer given by $\mathrm{ee}_{n-mer} = \frac{\chi_L^n - \chi_D^n}{\chi_L^n + \chi_D^n}$. On the other extreme, a stereospecific polymerization yields purely isotactic peptides and the final ee of n-mer would equal the starting monomer ee, with no chiral amplification. Therefore a prebiotic mechanism of chiral amplification must rely on other factors than stereoselectivity in the polymerization. The obvious answer considering the above is to isolate long isotactic peptides. Luisi and co-workers have shown that the statistical amplification of ee in isotactic polymers described above, combined with selective absorption of isotactic peptides onto quartz can improve the chiral amplification for leucine [9].

The low solubility of isotactic peptides compared to atactic peptides is due to their ability to form β-structured amyloid-like aggregates. We show that under prebiotic polymerization conditions [10] that L-alanine and L-valine form amyloid-like structures and that racemic mixtures of these amino acids polymerize to form β-rich aggregates. Therefore, the selective aggregation of isotactic peptides from racemic polymerization reactions likely involves amyloid-like structures. We have investigated the roles of the prebiotic amino acids glycine, alanine, valine and aspartate in the amplification of chirality in polymerizations starting from scalemic mixtures with low ee. Interestingly, the lower the concentration of amino acids during polymerization, the better the amplification of ee in the precipitate. Also, the tendency of valine to form racemic β-sheets limits the ee enhancement that can be achieved with this amino acid alone. Alanine which we found does not form racemic β-sheets yields better ee enhancement but due to its lower tendency to aggregate requires longer polymers. Our results indicate that combinations of valine which provides for significant aggregation propensity and alanine which limits the tendency to form racemic aggregates should yield even better ee enhancement via the above mechanisms and other mechanisms that will be discussed.

References:

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