

## Elucidation of the Absolute Structures of Putisolvins I and II

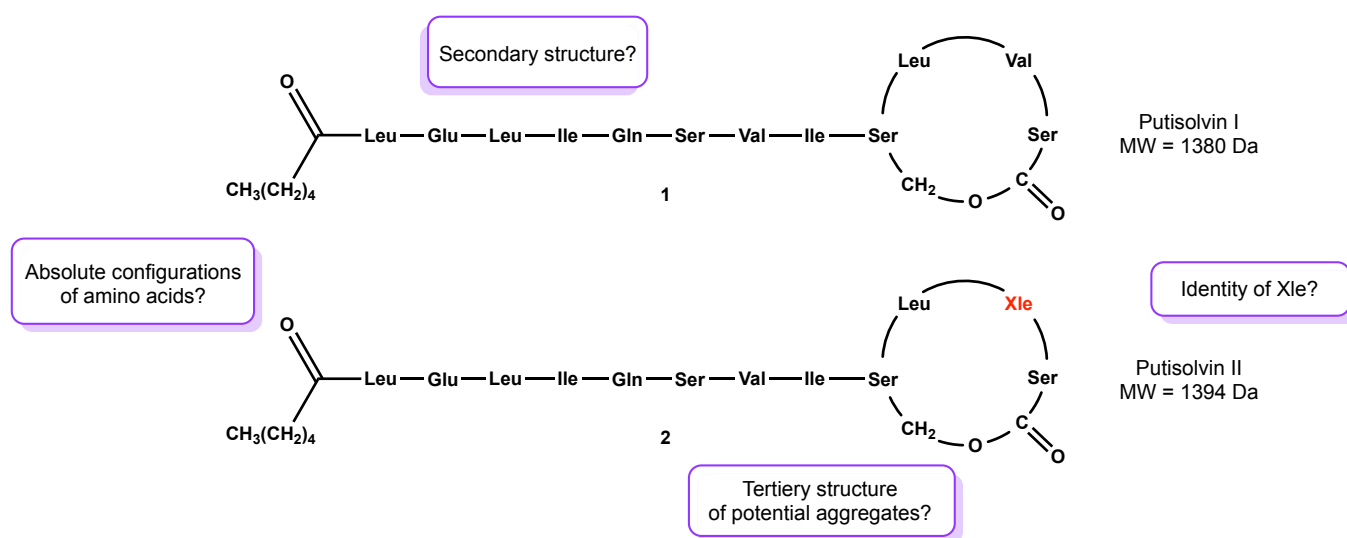
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Putisolvins I and II are the lipopeptides produced by *Pseudomonas putida* PCL1445 through non-ribosomal peptide synthesis and were first isolated in Bloemberg's group in 2004.<sup>[1]</sup> These cyclic lipopeptides display surface-tension reducing activity and the potential to inhibit biofilm formation. The structures of the compounds were subjected to NMR, ES-CID tandem MS, and amino acid analyses and were reported to consist of 12 amino acids, a fatty acid, and contain a macrocycle (figure 1). The MS and NMR analyses revealed the difference in one amino acid in the macrocycle, suggesting the presence of either Ile or Leu (abbreviated as Xle).<sup>[1,2]</sup>



**Figure 1.** Structures of Putisolvin I (1) and Putisolvin II (2)

However, several structural issues remain and were addressed in this study: (1) the absolute configuration of the constituent amino acids; (2) the identity of Xle; (3) the secondary structure of these lipopeptides, and (4) the tertiary structure of potential aggregates. We have performed chemical, analytical, physical, biological, and computational approaches to investigate these challenges, such as chemical and enzymatic degradation, UHPLC-MS on chiral stationary phases, 2D NMR spectroscopy, H/D exchange, CD spectroscopy, and computational studies (DP4+ and molecular dynamics).

1. I. Kuiper, E.L. Lagendijk, R. Pickford, J.P. Derrick, G.E.M. Lamers, J.E. Thomas-Oates, B.J.J. Lugtenberg, G.V. Bloemberg, *Mol. Microbiol.*, **2004**, *51*, 97–113;
2. J.F. Dubern, E.R. Coppoolse, W.J. Stiekema, G.V. Bloemberg, *Microbiology*, **2008**, *154*, 2070–2083.