Structural studies of adipokinetic hormones in water and DPC micelle solution using NMR distance restrained molecular dynamics

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Abstract

Melme-CC (pGlu-Leu-Asn-Tyr-Ser-Pro-Asp-Trp amide) and Declu-CC (pGlu-Leu-Asn-Phe-Ser-Pro-Asn-Trp-Gly-Asn amide) are members of the insect adipokinetic hormone family with very different activities in the locust bioassay. The conformations of both peptides were determined in water and in a phospholipid (DPC) micelle solution using nuclear magnetic resonance (NMR) restrained molecular dynamics simulations.

In water, Melme-CC has one dominant conformation while in DPC solution it has two preferred conformation. In water, Declu-CC has two conformations but in DPC solution it has one preferred conformation, which is similar to one of the water conformations. All the conformations have type IV β-turn between residues 4 and 7.

The binding of the two peptides to the DPC micelle is different. Melme-CC does not bind strongly to the surface and is oriented with the β-turn facing the surface. Declu-CC interacts more strongly with the β-turn facing away from the surface. Both termini having hydrophobic interactions with the surface. In Declu-CC the side chain of Asn7 projects away from the chain while in Melme-CC the Asp7 side chain is folded inside the chain. The different orientation of these side chains may account for the much higher biological activity of Declu-CC in mobilizing lipids in the locust compared to the poor biological effect of Melme-CC in this bioassay. Receptor binding of Declu-CC was tested using a model AKH receptor from Anopheles gambiae. A free energy of binding of −38.5 kJ mol−1 was found.