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Spatial structure of heptapeptide Glu-Ile-Leu-Asn-His-Met-Lys, a fragment of the HIV enhancer prostatic acid phosphatase, in aqueous and SDS micelle solutions

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HIGHLIGHTS

- Central region of Prostatic Acid Phosphatase peptide was synthesized and characterized.
- Spatial structure of the peptide in water and in complex with sodium dodecyl sulfate was revealed.
- Complex formation was confirmed by ^{1}H NMR spectra.

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ABSTRACT

Prostatic acid phosphatase (PAP) is a protein abundantly present in human seminal fluid. PAP plays important role in fertilization. Its 39-amino-acid fragment, PAP(248–286), is effective in enhancing infectivity of HIV virus. In this work, we determined the spatial structure in aqueous solution of a heptapeptide within the PAP fragment, containing amino acid residues 266–272 (Glu-Ile-Leu-Asn-His-Met-Lys). We also report the structure of the complex formed by this heptapeptide with sodium dodecyl sulfate micelles, a model of a biological membrane, as determined by ^{1}H NMR spectroscopy and 2D NMR (TOCSY, HSQC-HECADE, NOESY) spectroscopy. Complex formation was confirmed by chemical shift alterations in the ^{1}H NMR spectra of the heptapeptide, as well as by the signs and values of NOE effects. We also present a comparison of the spatial structure of Glu-Ile-Leu-Asn-His-Met-Lys in water and in complex with sodium dodecyl sulfate.

1. Introduction

Prostatic acid phosphatase (PAP) is present in human seminal fluid and nearest tissue in large quantities [1]. PAP has been shown to have an important role in human normal physiological and pathological processes, such as fertilization, prostate carcinoma, and HIV infection [1–3]. A 39-amino-acid fragment within PAP, PAP(248–286), forms amyloid fibrils [1] that can greatly increase the risk of HIV infection, promoting virus attachment to the host cell [3]. These amyloid fibers, known as Semen-derived Enhancer of Viral Infection (SEVI), are thought to act as polycationic bridges, neutralizing the negative charge (the charge on the membrane surface) between the viral capsid and the host cell membrane [4]. However, the mechanism of action of PAP is still poorly understood.

The central region of PAP(248–286) is a heptapeptide, Glu-Ile-Leu-Asn-His-Met-Lys (EILNHMK, PAP(266–272)). Studying the interaction of the heptapeptide with the cellular membrane may be useful for understanding the mechanism of activity of PAP as a whole. The aim of this work was to determine the spatial structure of EILNHMK in complex with sodium dodecyl sulfate (SDS) micelles, which represent a cell surface membrane model. In this investigation, we have used high-resolution NMR spectroscopy, which is highly suitable for these studies, and several variations of this technique. Elucidating the spatial structure of the complex heptapeptide-SDS, as well as the structure of the heptapeptide in solution, may allow us to understand the mechanism(s) of PAP protein interaction with the cell surface. This work will lay the foundation for developing effective medications to inhibit the binding of HIV or other viral agents to the eukaryotic cell membrane.

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