Solution structure and in Silico binding of a cyclic peptide with hepatitis B surface antigen

ABSTRACT

A specific ligand targeting the immunodominant region of hepatitis B virus is desired in neutralizing the infectivity of the virus. In a previous study, a disulfide constrained cyclic peptide cyclo S1,S9 Cys-Glu-Thr-Gly-Ala-Lys-Pro-His-Cys (S1, S9-cyclo-CETGAKPHC) was isolated from a phage displayed cyclic peptide library using an affinity selection method against hepatitis B surface antigen. The cyclic peptide binds tightly to hepatitis B surface antigen with a relative dissociation constant (KDrel) of 2.9 nm. The binding site of the peptide was located at the immunodominant region on hepatitis B surface antigen. Consequently, this study was aimed to elucidate the structure of the cyclic peptide and its interaction with hepatitis B surface antigen in silico. The solution structure of this cyclic peptide was solved using 1H, 13C, and 15N NMR spectroscopy and molecular dynamics simulations with NMR-derived distance and torsion angle restraints. The cyclic peptide adopted two distinct conformations due to the isomerization of the Pro residue with one structured region in the ETGA sequence. Docking studies of the peptide ensemble with a model structure of hepatitis B surface antigen revealed that the cyclic peptide can potentially be developed as a therapeutic drug that inhibits the virus–host interactions.

Keyword: Cyclic peptide; HBsAg; Immunodominant region; Modeling; NMR.