SYNTHESIS OF PEPTIDE FRAGMENTS OF THE VP1 PROTEIN OF HEPATITIS A VIRUS

Yu. A. Semiletov, M. G. Petrova, and V. D. Smirnov

UDC 577.964.4:577.112.6

In connection with investigations directed to obtaining synthetic vaccines against hepatitis A virus, we have performed the synthesis of two undecapeptides having the amino acid sequences of the proposed antigenic determinants of the surface protein VP1 of hepatitis A virus, namely:

H-Thr-Phe-Asn-Ser-Asn-Asn-Lys-Glu-Tyr-Thr-Phe-OMe (99—109) (I)

H-Ser-Thr-Ser-Asn-Pro-Pro-His-Gly-Leu-Pro-Ser-OH (115—125) (II)

The choice of fragment 99-109 and 115-125 was made on the basis of the amino acid sequence determined for the capsid proteins of hepatitis A virus [1, 2] and of a calculation of the secondary structure and distribution of the VP1 protein and also in the light of literature information [3, 4] showing that the VP1 protein is the most exposed of the structural proteins of the virus and contains virion-neutralizing sections.

The peptides were synthesized in solution using schemes combining the stepwise growth of the peptide chain by the activated pentafluorophenyl ester method [5] and the block condensation of peptide fragments 99-105 and 106-109 in the case of peptide (I) and fragments 115-117, 118-120, and 121-125 for peptide (II) by the azide method (all the amino acids were of the L-configuration). Activated p-nitrophenyl esters were used to introduce the asparagine residues. The tert-butoxycarbonyl (BOC) group was used as a temporary N^{α}-protective group in the synthesis of all the peptides. The lateral functions of the trifunctional amino acids, apart from histidine, were protected by groups stable under the conditions of eliminating the BOC protection and were eliminated simultaneously by the action of 1 M trifluoro-methanesulfonic acid—anisole in trifluoroacetic acid [6], the O-benzyl group for Tyr and Ser, the γ-benzyl ester group for Glu, and the ε-benzyloxycarbonyl group for Lys. The imidazole ring of histidine was protected by a BOC group. The Thr and, in the case of peptide (I), Ser residues were introduced into the peptide chain with unprotected hydroxy groups.

After purification by reversed-phase HPLC the following were obtained: the bistrifluoroacetate of peptide (I) with a yield of 48%, $[\alpha]_D^{29}$ −30.4° (c 0.5; H_2O); and the bistrifluoroacetate of peptide (II) with a yield of 55%, $[\alpha]_D^{29}$ −98.8° (c 0.5; H_2O). The chemical individuality of the compounds was confirmed by the results of amino acid analysis and by TLC on silica gel.

LITERATURE CITED

1. Yu. A. Ovchinnikov, E. D. Sverdlov, S. A. Tsarev, S. G. Arsenyan, and T. O. Rokhlina, Dokl. Akad. Nauk SSSR, 285, 1014 (1985).
2. D. L. Linemeyer, J. G. Menke, A. Martin-Gallardo, J. V. Hughes, and A. Young, J.Virol., 54, 277 (1985).
3. J. V. Hughes, L W. Stanton, I. E. Tomassini, W. J. Long, and E. M. Scolnick, J. Virol., 52, 465 (1984).
4. E. A. Emini, J. V. Hughes, D. S. Perlow, and J. Boger, J. Virol., 55, 836 (1985).
5. L. Kisfaludy, M. Takeyama, J. Kanaki, and K. Mitahi, J. Chem. Soc. Chem. Communs., 482 (1978).
6. H. Yajima, M. Takeyama, J. Kanaki, and K. J. Mitahi, J. Chem. Soc., Chem. Commun., 482 (1978).

D. I. Ivanovskii Institute of Virology, Moscow. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 152-153, January-February, 1987. Original article submitted July 16, 1986.

0009-3130/87/2301-0131$12.50