THE CHEMICAL STRUCTURES OF STREPTOVIRUDINS

Sir:

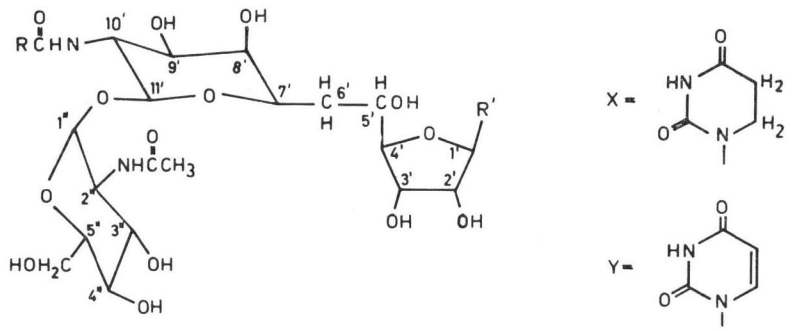
Streptovirudins are nucleoside antibiotics that were found to be chemically and biologically related to tunicamycins. Recently, the antibiotic complexes were differentiated by HPLC and gel chromatography.[1] In this communication, we wish to report on the chemical structures of the streptovirudins.

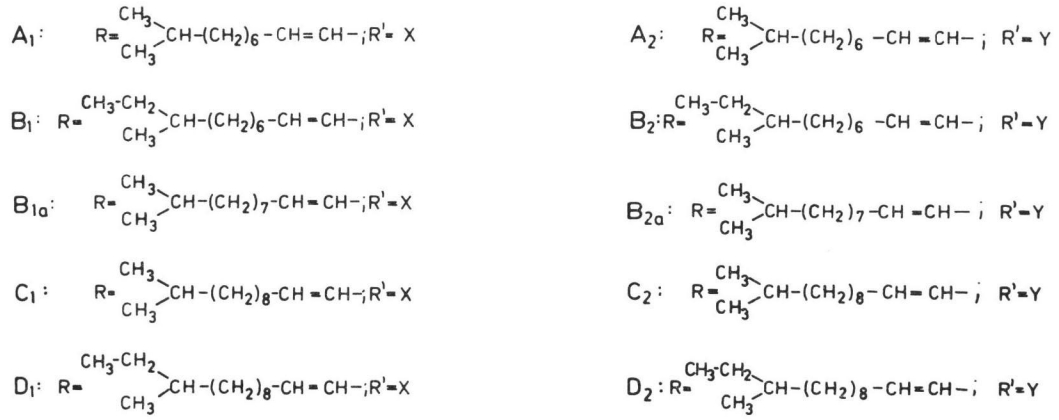
The molecular weights of streptovirudins have been determined by FD mass spectrometry as follows: A_1: 790, A_2: 788, B_1: 804, B_2: 802, C_1: 818, C_2: 816.[2] Acid hydrolysis under different conditions afforded several degradation products. In previous studies we found, that hydrolysates of all streptovirudins contained glucosamine identified as α-D-glucosamine. According to the NMR spectra, the aminosugar is present in the molecules of all streptovirudins as *N*-acetyl-D-glucosamine.

In regards to their different spectral properties the streptovirudins have been separated into two distinct series (series I: A_1, B_1, C_1, D_1; series II: A_2, B_2, C_2, D_2). Streptovirudins of series II show an UV maximum at 259 nm which is due to an uracil moiety in their molecules. Uracil was isolated from series II hydrolysates by Sephadex chromatography and was identified by mass spectrometry. Streptovirudins of series I show no UV light absorption in the range 200~300 nm. Recently, we found that streptovirudins of this type contain dihydrouracil in place of uracil.[2,3]

In order to determine the nature of the fatty acid residues we investigated hydrolysates of streptovirudin complex and of the individual components following similar lines as described by TAKATSUKI *et al.*[4] After hydrolysis with 6 N HCl the liberated fatty acids were converted into their methyl esters and then analysed by GLC-MS. The methyl esters of the following acids were identified: 10-methyl-2-undecenoic acid, 10-methyl-2-dodecenoic acid, 12-methyl-2-tridecenoic acid, 12-methyl-2-tetradecenoic acid. The structures were deduced mainly from the mass spectral data and could be confirmed by analysis of ^1H and ^{13}C NMR spectra of the

Fig. 1. Chemical structures of streptovirudins.





streptovirudins. As to be seen in Fig. 1, the corresponding pairs A_1/A_2, B_1/B_2, C_1/C_2 and D_1/D_2, respectively, contain identical fatty acid residues. Contrary to tunicamycins the streptovirudins contain only unsaturated iso and anteiso acids.

The complete structures shown in Fig. 1 have been derived from the NMR spectra of the pure components. ITO *et al.*[5] have shown that all tunicamycins contain tunicamine as the central moiety in their molecules. The assignment of a representative ^1H NMR spectrum has been published by the authors based on the results obtained from the investigation of tunicaminyl uracil. When we compared the ^1H NMR data of tunicamycin with those of streptovirudins, in the range $1.8 \sim 8$ ppm all characteristic signals assigned by ITO *et al.* were found in the spectra of series II streptovirudins suggesting the same structures of the uracil-carbohydrate parts. Analogous conclusions were made with series I streptovirudins taking into account the characteristic differences that are due to the presence of dihydrouracil in place of uracil. Up to now, no ^{13}C NMR spectra of tunicamycins or streptovirudins have been published. We measured the 200 MHz ^{13}C spectra of the streptovirudins. The assignment of the spectra gave strong support for the structures depicted in Fig. 1. Detailed results will be published elsewhere.

A discrepancy was found as the ^{13}C NMR spectra of streptovirudins B_1 and B_2 contained two unexpected additional signals characteristic of isomeric compounds. From consideration of both ^{13}C NMR and ^1H NMR spectra it has been inferred that streptovirudin B_1 contained about 20% of compound B_{1a} and, similarly, streptovirudin B_2 about the same amount of streptovirudin B_{2a} (Fig. 1). According to the chemical structures only streptovirudins C_2 and B_{2a} are identical with tunicamycin factors.

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References

1) ECKARDT, K.; H. WETZSTEIN, H. THRUM & W. IHN: Streptovirudin and tunicamycin, two inhibitors of glycolipid synthesis. Differentiation by use of gel chromatography, HPLC and hydrolysis. J. Antibiotics 33: 908~910, 1980
2) ELBEIN, A. D.; J. OCCOLOWITZ, R. HAMILL & K. ECKARDT: Streptovirudins of series I and II. Chemical and biological properties. Biochemistry 20: 4210~4216, 1981
3) ECKARDT, K.; W. IHN, D. TRESSELT & D. KREBS: On the chemical structures of streptovirudins. Presence of dihydrouracil in streptovirudins A_1, B_1, C_1, D_1. Proc. 1st Int. Conf. Chem. Biotechnol. Biol. Act. Nat. Products. Varna, 1981
4) TAKATSUKI, A.; K. KAWAMURA, Y. KODAMA, T. ITO & G. TAMURA: Structure determination of fatty acids from tunicamycin complex. Agric. Biol. Chem. 43: 761~764, 1979
5) ITO, T.; A. TAKATSUKI, K. KAWAMURA, K. SATO & G. TAMURA: Isolation and structures of components of tunicamycin. Agric. Biol. Chem. 44: 659~698, 1980