THE TRANSGLYCOSYLATION OF KANAMYCIN A

Sir:

In our previous paper in this series[1] we reported the transglycosylation of neamine (to form 5-glucosylneamine) which resulted in increased antibiotic potency *in vitro*. We have extended PAN's system[2] to other antibiotics and wish to report our observations on glycosylated kanamycin A.

This material was prepared by adding 1 g kanamycin A[3], 4 g maltose, and 1 g Clarase^R to 40 ml of McILVAINE's pH 4.0 buffer and incubating the solution for 96 hours at 50°C. After this period new ninhydrin-positive and biologically active components were observed upon paper ionophoresis of the mixture (pH 1.8, 53 volts/cm, 20 minutes) and in silica gel thin-layer chromatography (using $CHCl_3$-MeOH-NH_4OH, 1:3:2).

The reaction mixture was diluted 3-fold with water and the pH adjusted to 8 with NaOH. The diluted solution was then passed through CG 50 resin (NH_4^+ cycle, 30 ml column). The biologically active components (against *Staphylococcus aureus*) were eluted with NH_4OH gradient of 0~0.5 N NH_4OH. The crude material was purified by rechromatographing on CG 50 (NH_4^+ cycle, 50 ml column) using 0.1 N NH_4OH as eluting solution, and the active fractions were lyophilized.

Analysis of the purified material gave C, 40.20%, N 7.85%. The C/N ratio of 5.9 is close to the C/N ratio of 6.0 expected for a glycosylated kanamycin A. The biological activity of this material was considerably less than the kanamycin A, having about 50% of the activity against *Bacillus subtilis* Marburg, and less than 1% against *S. aureus* FDA 209P, *Sarcina lutea*, *Escherichia coli*, and *Pseudomonas aeruginosa*. *In vivo* studies showed the kanamycin A derivative had about 25% of the activity of the parent compound in mice infected with *S. aureus*, and less than 1% of the activity of the parent compound in mice infected with *E. coli*.

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