NOTES

AMIDINOMYCIN FROM *STREPTOMYCES KASUGAENSIS* PRODUCING KASUGAMYCIN

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It was reported that in addition to kasugamycin, aureothricin, thiolutin and a polyene antifungal substance were produced by *Streptomyces kasugaensis*[1]. In the course of studying production of kasugamycin on various media, another antibiotic was found in a culture broth of this *Streptomyces*. The antibiotic, weakly active against *Bacillus subtilis*, was isolated by an ion-exchange resin method and identified as amidinomycin[2,3] (myxoviromycin[4]).

An antibiotic active against *B. subtilis* was detected in the culture broths of three strains out of five which had been obtained by repeated monospore isolation with or without ultraviolet irradiation. This antibiotic was not extracted with ethyl acetate and appeared in the eluate with 0.5 N hydrochloric acid from ion-exchange resin (Amberlite IRC-50 (Na^+ type)) chromatography of the antibiotic.

For the production of the antibiotic, soybean meal, corn steep liquor, cotton meal, peptone and meat extract were tested as nitrogen sources and glucose, maltose, glycerol, starch, lactose and soy oil as carbon sources. Soybean meal and glycerol were the most suitable. The medium for the production of the antibiotic was as follows: 2.0 % glycerol, 1.5 % soybean meal, 0.1 % K_2HPO_4, 0.05 % $MgSO_4 \cdot 7H_2O$ and initial pH was not adjusted.

After incubation for 70 hours at 27°C, the fermented broth was adjusted to pH 7.6 and filtered. The antibiotic in the filtrate was adsorbed on Amberlite IRC-50 (Na^+ type). The active eluate with 0.5 N hydrochloric acid was lyophilized to a white powder. The powder was chromatographed on active carbon and Amberlite IRC-50 (H^+ type). The antibiotic was eluted with 0.5 N sulfuric acid. The active eluate was concentrated and treated with ethanol, yielding a crude crystalline precipitate. The crude sulfate was recrystallized from aqueous ethanol. There was obtained 3.2 g of the colorless sulfate from 27.8 liters of the filtered broth. The overall yield was about 24 %.

The sulfate darkens at 260°C and melts at 280~285°C (decomp.), $[\alpha]_D^{25}$ −2.3° (*c*, 5.33 in water). Its analytical data are identical with that of amidinomycin, calcd. for $C_9H_{18}N_4O \cdot H_2SO_4$: C 36.47, H 6.80, N 18.90, O 26.99, S 10.82; found: C 35.75, H 6.77, N 18.12, O 27.83, S 10.93. The identity with amidinomycin was confirmed by no depression of the mixed melting point and the same infrared spectrum as an authentic sample of amidinomycin in a potassium bromide pellet. The structure of amidinomycin, N-(2′-amidinoethyl)-3-aminocyclopentanecarboxamide was supported by the n. m. r. spectrum of its deuterium oxide solution.

References

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