HENEICOMYCN, A NEW ANTIBIOTIC (A21A):
FERMENTATION, ISOLATION,
AND ANTIBACTERIAL SPECTRUM

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In the course of our screening for new antibiotics, we have found heneicomycin (antibiotic A21A)\(^1\) in culture broth of a newly isolated strain of *Streptomyces filipinensis*, designated NRRL #11044 (MA-4581 in the Merck & Co., Inc. culture collection).

From the physico-chemical and biological properties described in this communication, heneicomycin is considered to be equivalent to 3-deoxyaurodox (Fig. 1), a new antibiotic belonging to the aurodox (X5108)\(^2\) - kirromycin\(^3\) group.

Heneicomycin, which is active *in vitro* vs both Gram-positive and Gram-negative organisms (Table 1), is produced by cultivating *S. filipinensis* NRRL 11044 under submerged, aerobic conditions in aqueous medium containing 4% tomato paste and 1.5% ground oatmeal, with pH adjusted to 6.0 with NaOH. Production of the antibiotic reached a maximum after 5 days' incubation at 28°C on a rotary shaker at 220 rpm.

The culture broth containing heneicomycin was filtered through Celite and the filtrate was adjusted to pH 5.0 with hydrochloric acid before extraction with ethyl acetate. The ethyl acetate extract was triturated with *n*-hexane thereby precipitating heneicomycin. The resulting precipitate was subjected to preparative silica-gel thin-layer chromatography using chloroform, methanol, and concentrated aqueous NH\(_3\) (80: 20: 1.5) as a developing solvent. The major band, which was bright yellow in color, was extracted with a mixture of chloroform, methanol, and distilled water (60: 30: 3). The solution was concentrated, redissolved in benzene - methanol (95: 5) and lyophilized, yielding heneicomycin as an amorphous bright yellow powder which was soluble in methanol and ethanol and slightly soluble in chloroform and acetone. Heneicomy-

![Fig. 1. Structure of heneicomycin.](image_url)
cin has prominent characteristic absorption peaks at approximately \( \lambda \) (0.01 N HCl in methanol) = 322 nm, \( \varepsilon \% = 328 \); and 231 nm, \( \varepsilon \% = 722 \). Combustion analysis gave C 65.23 %, H 7.78 %, and N 3.47 %, values consistent with \( \text{C}_{44}\text{H}_{62}\text{N}_{2}\text{O}_{11} \cdot \text{H}_{2}\text{O} \). The UV, IR, and NMR spectra are shown in Figs. 2, 3, and 4, respectively. The NMR spectrum was taken in deuterated CHCl_3, with trimethylsilane as internal reference. The field desorption mass spectrum showed peaks at \( m/e \) 794 (M\(^+\)) as well as \( m/e \) 795 (M\(^+\)H\(^+\)) and 817 (M\(^+\)Na\(^+\)). The electron impact mass spectrum showed peaks (relative intensities in parentheses) at \( m/e \) 680 (0.6), 648 (2.1), 630 (0.8), 594 (1.0), 483 (1.7), 481 (1.1), 465 (1.1), 463 (0.8), 384 (6.7), 338 (6.3), 306 (4.6), 302 (9.4), 275 (10.5), 274 (9.2), 245 (33), 192 (36), 181 (23), 179 (21), 166 (33), 152 (100), 135 (21), 133 (13), 123 (92), 121 (19), 119 (25), 108 (35), 107 (36), 97 (94). The trimethylsilyl derivative showed peaks up to \( m/e \) 1226 (M\(^+\) + 6TMS). The above physical properties together with a detailed spectral examination indicated that heneicomycin was a new antibiotic, namely the 3-deshydroxy pyran modification of aurodox.

A solution of 1,000 \( \mu \)g/ml of heneicomycin in 40% acetone-distilled water demonstrated a broad antibacterial spectrum (Table 1), using a sample droplet of 0.015 ml on the surface of seeded agar plates containing nutrient agar. The 40% acetone-water solution alone demonstrated no inhibition with any of the test organisms. Of all organisms tested, \textit{Mycoplasma gallisepticum} S-6 was the most susceptible.

References