IDENTITY OF BORRELIDIN WITH TREPONEMYCIN

HUBERT MAEHR and RALPH H. EVANS

Roche Research Center,
Hoffmann-La Roche Inc.,
Nutley, N.J. 07110, U.S.A.

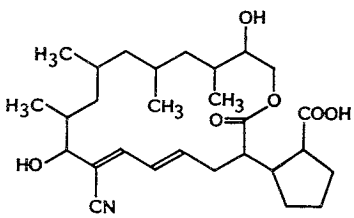
(Received for publication April 20, 1987)

Treponemycin has recently been described as a novel antibiotic, produced by *Streptomyces albovinaceus* with activity against *Treponema hyodysenteriae* and featuring lactone and/or ester groups, as well as a nitrile conjugated with a diene, but lacking hydroxyl and carboxyl functions.[1]

Upon detailed examination of the published data on treponemycin we came to the conclusion that treponemycin is actually identical with borrelidin, an antibiotic discovered much earlier as a metabolite of *Streptomyces rochei*[2] and *Streptomyces* sp. C2989.[3] Borrelidin was chemically characterized[2,4] and identified as 2-[7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]cyclopentanecarboxylic acid[5] as shown below (Fig. 1).

Comparing the data on borrelidin with those available on treponemycin reveals identical molecular formulas of $C_{28}H_{43}O_6N$ both by elemental analysis and mass spectrometry and similar optical rotations ($[\alpha]_D$ $-28°$ [2] and $-28.8°$ [4] in ethanol for borrelidin and $-17.47°$ in chloroform for treponemycin,[1] respectively). There are no differences between the reported UV spectral data of the two compounds and all characteristic IR bands reported for borrelidin could be observed in the spectrum of treponemycin, including those indicative of hydroxyl and carboxyl groups. Further, the reported NMR spectrum of treponemycin[1] is fully compatible with that of borrelidin in the light of the following reinterpretation: The three signals at δ 0.79, 0.82 and 0.85 do not represent methyl groups at quaternary carbons but are a composite of three methyl groups at methine carbons. The signal at δ 1.25 does not represent a methyl group but is due to an alkane impurity and the doublet at δ 1.04 is not derived from a geminal dimethyl group but is actually generated by a fourth CH_3CH function.

Fig. 1.



Borrelidin

We had the opportunity to compare authentic samples of borrelidin and treponemycin† and found no differences in silica gel TLC comparisons using the following solvent systems (Rf): Diethyl ether - hexane - acetone - ethanol, 70:30:10:2.5 (0.18); hexane - tetrahydrofuran, 1:1 (0.40); dichloromethane - hexane - ethanol, 8:2:1 (0.51); ethyl acetate (0.55); ethyl acetate - hexane - methanol, 15:5:1 (0.56); dichloromethane - methanol, 9:1 (0.90). Borrelidin and treponemycin gave single peaks with identical retention times of 8.15 minutes upon reverse-phase HPLC (column: 25×4.5 mm, C_{18}-phase, ODS-3, 5 μm, Whatman; mobile phase: Methanol - 1% acetic acid, 3:1; flow rate: 0.9 ml/minute UV-detection at 257 nm).

Direct IR, NMR and mass spectral comparisons of borrelidin and treponemycin did not dispute the identity of the two substances, but indicated different degrees of purity. The difference in the reported mp of 145~146°C and 93~95°C for borrelidin and treponemycin, respectively, can be attributed to different purity grades and physical states. Whereas borrelidin was described as a crystalline substance, our authentic treponemycin sample was an amorphous solid with mp 93~100°C.

References

1) SINGH, S.K.; S. GURUSIDDAIAH & J.W. WHALEN: Treponemycin, a nitrile antibiotic active against *Treponema hyodysenteriae*. Antimicrob. Agents Chemother. 27: 239~245, 1985

2) BERGER, J.; L. M. JAMPOLSKY & M. W. GOLDBERG: Borrelidin, a antibiotic with antiborrelia activity and penicillin enhancement properties. Arch. Biochem. Biophys. 22: 476~478, 1949

† Borrelidin was obtained from our antibiotic collection. We thank Dr. GURUSIDDAIAH for a sample of treponemycin.

3) LUMB, M.; P. E. MACEY, J. SPYVEE, J. M. WHITMARSH & R. D. WRIGHT: Isolation of vivomycin and borrelidin, two antibiotics with anti-viral activity, from a species of *Streptomyces* (C2989). Nature 206: 263~265, 1965

4) ANDERTON, K. & R. W. RICKARDS: Some structural features of borrelidin, an anti-viral antibiotic. Nature 206: 269, 1965

5) KELLER-SCHIERLEIN, W.: Die Konstitution des Borrelidins. Experientia 22: 355~359, 1966