NOTES

IDENTITY OF THE ANTITUMOR ANTIBIOTIC LITMOMYCIN WITH GRANATICIN A

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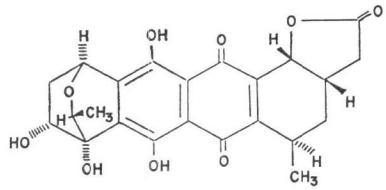
The antibiotic litmomycin has been isolated from a new *Streptomyces* species, *S. litmogenes*[1]. The antibiotic, which is produced in yields of over 2 g/liter, is highly active against gram-positive bacteria (MIC 0.25~1.75 μg/ml), but has little or no activity against gram-negative bacteria, mycobacterium, molds or yeast[2].

Litmomycin was produced by fermentation of *S. litmogenes* on a peanut meal-starch medium for 48 hours. The whole culture was adsorbed on charcoal at pH 4.0 and filtered. The cake was washed with acidic water, air-dried, defatted with *n*-hexane and then extracted with acetone. The eluate was evaporated to dryness the residue dissolved in dilute ammonia (pH 8~9), and the solution was acidified and extracted with ethyl acetate. Repeated recrystallization of the residue of this extract from benzene gave pure litmomycin, m.p. 223~225°C. The antibiotic has the molecular formula $C_{22}H_{20}O_{10}$ (M.W. 444, calc. C 59.46%, H 4.54%, found C 59.41, H 4.72 %); its electron-impact mass spectrum shows fragment ions at *m/e* 400 ($C_{20}H_{16}O_9$) and 384 ($C_{20}H_{16}O_8$), whereas the NH_3 chemical ionization mass spectrum shows a peak at 447, presumably corresponding to a protonated molecular ion. Other spectroscopic data for litmomycin are: UV(EtOH) nm (log ε): 223 (5.30), 286 (4.57), 532 (4.62) and 5.76 (4.53); IR (KBr) cm^{-1}: 1770, 1600 and 1565; NMR (220 MHz, TFA) δ, ppm, (J, Hz): 1.25 (d, 7), 1.69 (d, 7), 1.89 (bd, 15), 3.00 (d, 15), *ca.* 3.02 (m), 3.34 (dd, 18.5), 4.23 (q, 7), 4.51 (d, 8), 5.01 (br. s), 5.34 (q, 7), 5.62(m). A comparison of litmomycin with known antibiotics by bioautography indicated that its behavior closely resembled that of granaticin, and antibiotic isolated from *Streptomyces olivaceus*[3]. Comparison of the spectroscopic data with those published for granaticin A[3,4] showed good agreement and a direct comparison of litmomycin with a sample of granaticin A kindly provided by Prof. H. ZÄHNER confirmed their identity.

Granaticin A (litmomycin)



Granaticin (litmomycin) has significant antitumor activity against P-388 lymphocytic leukemia in mice (T/C 166% at 1.5 mg/kg) and cytotoxicity against KB cells (ED_{50} 1.6 μg/ml).

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