Isolation and Characterization of Lunamycin, an Antitumoric Substance from Lampteromyces japonicus

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Lampteromyces japonicus (tsukiyotake) has long been well known in Japan as a poisonous mushroom. However, untill recently, the nature of the active principle has attracted

only little attention. In 1958, Nakai[1] concentrated a toxic material from this fungus and studied its pharmacological action, but could not obtain the toxin in a pure state. More recently, the active constituent of the mushroom has come to attract growing interest, since Komatsu and his coworkers[2] demonstrated a remarkable effect of extracts of the mushroom antagonistic to Ehrlich ascites carcinoma.

The writers wish to report the isolation of an active principle which exhibits antitumoric as well as toxic action[3], $C_{15}H_{22}O_4$, for which the name "Lunamycin" is suggested. Lunamycin was obtained in about 10^{-4}% yield from fresh mushrooms by careful, repeated chromatography through alumina of the ethyl acetate soluble, neutral part of the mushroom as a prismatic crystal, m. p. 122~124°C (Found: C, 67.78; H, 8.20; mol. wt. (micro Rast), 280. Calcd. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33%; mol. wt. 266. UV spectrum; λ_{max}^{EtOH} 235 mμ (log ε; 4.1), 325 mμ (log ε; 3.5). IR bands at 3500, 3400, 3280, 1692, 1660, 1602, 1107, 1026 cm^{-1}). Treatment of lunamycin with acetic anhydride and pyridine gave a diacetate, m. p. 98~99°C (Found: C, 65.38; H, 7.09; Calcd. for $C_{19}H_{26}O_6$; C, 65.12; H, 7.48%. UV spectrum; λ_{max}^{EtOH} 227 mμ (log ε; 4.1), 317 mμ (log ε; 3.5). IR bands at 3480, 1730, 1695, 1650, 1605, 1230, 1110, 1035 cm^{-1}). Thus lunamycin seems to have one conjugated carbonyl, two acylable hydroxyl and one hindered or tertiary hydroxyl groups. In certain cases a crystal $C_{15}H_{20}O_4$, m. p. 179~181°C (Found: C, 67.84; H, 7.28; mol. wt. (micro Rast), 281. Calcd. for $C_{15}H_{20}O_4$; C, 68.16; H, 7.63%; mol. wt. 264. UV spectrum; λ_{max}^{EtOH} 248 mμ (log ε; 4.3). IR bands at 3430, 3330, 1685 cm^{-1}) was isolated from a fraction eluted just before the most toxic part. This crystal exhibited rather low toxicity; injection of 26 mg. of sample killed a mouse in three days. The compound gave a triacetate, m. p. 110~111°C (Found: C, 64.68; H, 6.76; Calcd. for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71%. UV spectrum λ_{max}^{EtOH} 253 mμ (log ε; 4.3). IR bands at 1730, 1700, 1240 cm^{-1}) upon treatment with pyridine and acetic anhydride. The details of the procedure for isolation of lunamycin will be reported elsewhere.

1) K. Nakai, *Medicine and Biology*, **48**, 33, 103, 211 (1958); **49**, 129 (1958).

2) N. Komatsu, Y. Ogata, S. Nakazawa, I. Yamamoto, M. Hamada, H. Terakawa and T. Yamamoto; Lecture at the 34th Annual Meeting of the Japan Bacteriological Society, April, 1961.

3) Lunamycin kills a mouse in a dosis of 0.6 mg. within 12 hr. Daily administration of 5 γ lunamycin for 4 days completly cures a mouse transplanted with 2.5×10^6 Ehrlich ascites carcinoma cells. The treatment was started one day after the transplantation (private communication from Dr. N. Komatsu).

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Added in proof; Professor Koji Nakanishi of Tokyo University of Education also isolated a toxic material lampterol from the same mushroom. The two samples were proved to be identical by comparison of infrared spectra and m. p. s.