# AN ANTITUMOR ANTIBIOTIC PRODUCED BY *PENICILLIUM STIPITATUM* THOM; ITS IDENTITY WITH DUCLAUXIN

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During our screening program for substances with antitumor activity we found that the culture filtrate of *Penicillium stipitatum* THOM CBS 375.48 showed some activity against the EHRLICH's ascitic tumor *in vitro*[1]. One of the active substances ($PSX_2$) was isolated as white needles, m.p. 235~236°C, $[\alpha]_D^{28}$ +322.7° (*c* 0.05, $CHCl_3$). The UV spectrum indicates the presence of some conjugated system. According to the IR spectrum in the 1600~1800 $cm^{-1}$ region, there are carbonyls of several kinds in the molecule. High resolution mass determination (peak-matching technique, PFK standard, accuracy better than 2 ppm) revealed the elemental composition $C_{29}H_{22}O_{11}$. Comparing the observed PMR spectrum (Tesla BS 487, 80 MHz, $CDCl_3$) with those of known fungal metabolites of the same formula, we found a reasonable agreement with the PMR spectrum of duclauxin[2,3], a metabolite produced by *Penicillium duclauxii*. Our compound also gave all colour reactions described for duclauxin[2]. The comparison with an authentic sample (kindly provided by Prof. SHIBATA) showed an identical TLC behaviour, indistinguishable mass spectra and only slightly different PMR spectra (measured under the same conditions). The chemical shift deviations can be explained by concentration and hydrogen bonding effects and the difference in the $[\alpha]_D$ values might be due to the different degree of purity. Therefore, the new metabolite of *P. stipitatum* is identical with duclauxin. However, some assignments in the PMR spectrum (Fig. 1a) should be revised according to our experiments (Fig. 1b). Two of the four methyl singlets (2.09 and 2.74 ppm)

Fig. 1. Assignment of the PMR spectra of duclauxin

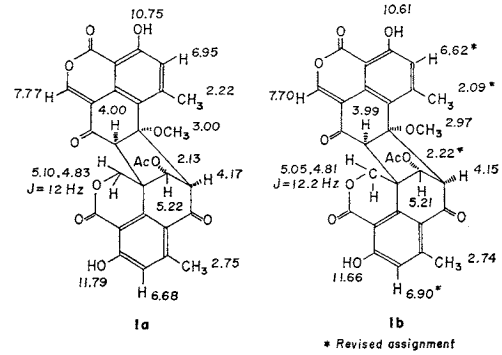
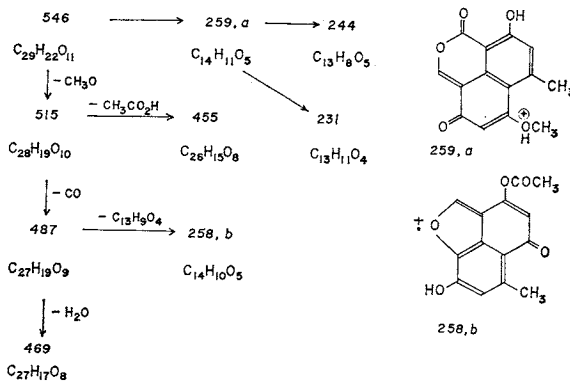



Fig. 2. Fragmentation pattern of duclauxin




are coupled to the aromatic protons at 6.62 and 6.90 ppm. Therefore, those signals are due to the olefinic methyls and the singlet at 2.22 ppm must be ascribed to the acetyl group. Since the upfield aromatic proton is coupled to the upfield aromatic methyl and the downfield aromatic proton is coupled to the downfield aromatic methyl, the assignment of the mentioned aromatic protons must be reversed with respect to the earlier one[3] The observed line shape of both aromatic methyl signals, known to reflect the double bond location[4,5], support this assignment. The mass spectrum (Varian MAT-311, 70 eV, direct inlet at 160°C (Fig. 2) can provide an additional tool for the identification of this compound. MS (*m/e*, % of relative abundance, elemental composition): 546 (11, $C_{29}H_{22}O_{11}$, $M^+$), 515 (2.1, $C_{28}H_{19}O_{10}$, $M-CH_3O$), 487 (3.2, $C_{27}H_{19}O_9$, $M-CH_3O-CO$), 469 (4.6, $C_{27}H_{17}O_8$, $487-H_2O$), 455 (8.9, $C_{26}H_{15}O_8$, $515-CH_3CO_2H$), 260 (18.5, $^{13}CC_{13}H_{11}O_5$), 259 (100, $C_{14}H_{11}O_5$, a), 258 (19.8, $C_{14}H_{10}O_5$, b), 246 (6.9, $C_{13}H_{10}O_5$), 244 (6.3, $C_{13}H_8O_5$), 243 (9.1, $C_{13}H_7O_5$), 231 (3.1, $C_{13}H_{11}O_4$), 230 (11.1,

$C_{13}H_{10}O_4$), 229 (6.7, $C_{13}H_9O_4$), 44 (17.3), 43 (24.7).

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