

## A NEW ANTIBIOTIC, TRICHORIN A

Sir:

In the course of screening antibiotics active against Gram-negative bacteria, we found a species of *Trichoderma* (strain K-472) produces a new antibiotic, trichorin A.

The fungus was fermented at 28°C for 72 hours on a reciprocal shaker using a Sakaguchi flask containing 100 ml of medium composed of 2% glucose, 1% peptone, 0.5% meat extract, and 0.3% sodium chloride at pH 7.0. The mycelial cake thus obtained was extracted with acetone and then ethyl acetate. The extracts were combined and evaporated *in vacuo*. The residue was dissolved in ethyl acetate, washed with 5% sodium carbonate, and evaporated *in vacuo* leaving a residue, which was dissolved in benzene and chromatographed on silica gel giving trichorin A and a small amount of trichorin B.

Trichorin A was obtained from acetone-*n*-hexane as colorless needles: C<sub>20</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub>S<sub>2</sub>; m.p. 234~246°C (dec.); [α]<sub>D</sub><sup>25</sup> -190.5° (dioxane); λ<sub>max</sub><sup>E<sup>1</sup>OH</sup> 205 nm (ε 38,000), 240 sh (11,000), and 280 sh (3,100); ν<sub>max</sub><sup>KBr</sup> 3490, 3330, 1715, 1685, 1606, 1508, 1215, 1101, 1025, 971, 831, 805, and 787 cm<sup>-1</sup>. Its CD curve showed COTTON effects at 225 nm ([θ] -55,400) and 291 nm ([θ] +7,450), and was similar to that of dehydrogliotoxin (I).<sup>1</sup> The presence of amide bands in the IR in conjunction with the negative COTTON effect at 225 nm indicates the presence of a dioxopiperazine<sup>2-4</sup> moiety in trichorin A. Moreover, trichorin A triacetate shows an ion at *m/e* 64 due to loss of S<sub>2</sub><sup>5</sup> in the mass spectrum, suggesting that it has a disulfide-bridged dioxopiperazine system and is a compound belonging to the gliotoxin group.<sup>4,6</sup>

When trichorin A was dissolved in pyridine for NMR examination it was converted into trichorin B, which had been obtained as a minor metabolite. Therefore, we prepared trichorin A triacetate by adding a small amount of pyridine

to a solution of trichorin A in acetic anhydride. The acetate was crystallized from methylene dichloride-ether-isopropyl ether to give colorless needles: C<sub>26</sub>H<sub>26</sub>N<sub>2</sub>O<sub>11</sub>S<sub>2</sub>; m.p. 212~214°C (dec.); ν<sub>max</sub><sup>CHCl<sub>3</sub></sup> 1780, 1729, 1609, 1088 and 1036 cm<sup>-1</sup>; λ<sub>max</sub><sup>E<sup>1</sup>OH</sup> 205 nm (ε 43,900), 240 sh (11,600) and 275 sh (3,600).

Trichorin B was obtained from ethanol as yellow plates: C<sub>20</sub>H<sub>20</sub>N<sub>2</sub>O<sub>8</sub>S; m.p. 230~238°C (dec.); ν<sub>max</sub><sup>KBr</sup> 3300, 1691, 1678, 1606, 1178, 1105, 1050, 992 and 810 cm<sup>-1</sup>; λ<sub>max</sub><sup>E<sup>1</sup>OH</sup> 248 nm (ε ca. 10,000) and 341 (ca. 20,000). Acetylation of trichorin B gave a triacetate: yellow prisms; C<sub>26</sub>H<sub>26</sub>N<sub>2</sub>O<sub>11</sub>S; m.p. 120~125°C (from ether); ν<sub>max</sub><sup>CHCl<sub>3</sub></sup> 3355, 1750, 1706, 1646, 1606, 1090, 1045 and 1033 cm<sup>-1</sup>; λ<sub>max</sub><sup>E<sup>1</sup>OH</sup> 246 nm (ε 14,100) and 327 (18,200).

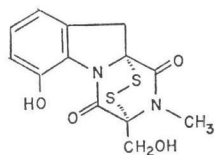
The combined results of <sup>1</sup>H NMR and <sup>13</sup>C FT NMR examination together with evidence from chemical degradation indicate that trichorin B triacetate has partial structure II, two acetoxy groups and a *cis*-disubstituted ethylenic double bond. Structural elucidation of trichorins A and B will be described elsewhere. Trichorin A has a weak activity against Gram-negative bacteria (MIC 50~100 μg/ml) and B has no activity.

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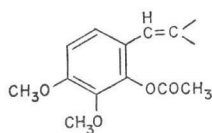
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