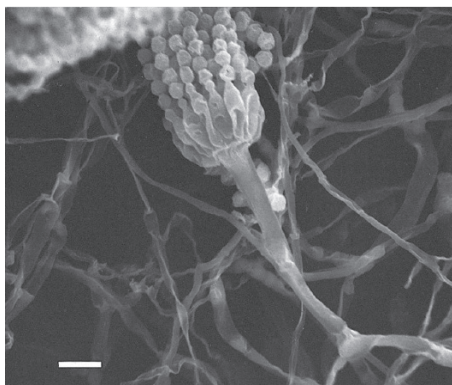


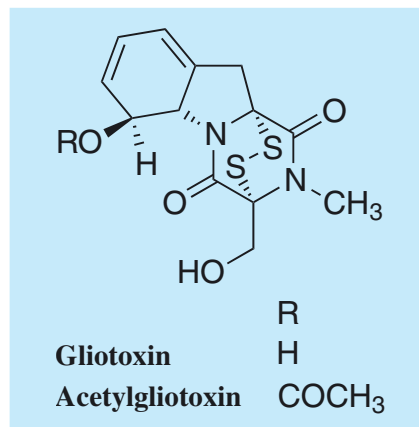
# Gliotoxin

## 1. Discovery, producing organism and structures<sup>1,7)</sup>

Gliotoxin and its acetyl derivative were isolated from the culture broth of the *Penicillium* fungal strain FO-2047. Gliotoxin is first inhibitor of protein farnesyltransferase of microbial origin. The total synthesis of gliotoxin was reported by Kishi *et al.*<sup>8,9)</sup> and Nicolaou *et al.*<sup>10)</sup> (See Appendix-I).



*Penicillium* sp. FO-2047  
Bar: 5  $\mu\text{m}$



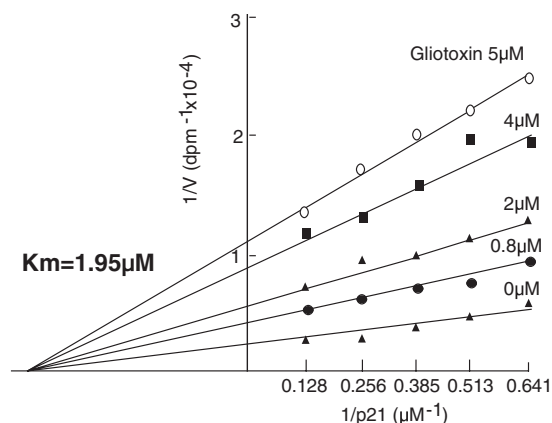
## 2. Physical data

White powder. C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>; mol wt 326.40. Sol. in DMSO, MeOH, CHCl<sub>3</sub>. Insol. in H<sub>2</sub>O.

## 3. Biological activity<sup>1-6)</sup>

### 1) Inhibition of protein farnesyltransferase<sup>1)</sup>

	IC <sub>50</sub> ( $\mu\text{M}$ )
Gliotoxin	1.1
Acetylgliotoxin	4.4



### 2) Other biological activities<sup>2-6)</sup>

Gliotoxin was discovered in 1932 as an antifungal agent<sup>2)</sup> when various biological activities were reported.

Antimicrobial activity<sup>3)</sup>:

Gliotoxin inhibited growth of a wide range of bacteria and fungi.

Antiviral activity<sup>4)</sup>:

Gliotoxin was shown to inhibit multiplication of RNA viruses by affecting the activity of RNA polymerase in cell cultures.

Immunomodulating activity<sup>5)</sup>:

Gliotoxin displayed antiphagocytic and other immunosuppressive properties.

PAF antagonist<sup>6)</sup>:

Gliotoxin derivatives were shown to inhibit platelet activating factor (PAF) which induced platelet aggregation.

#### 4. References

1. [494] D. Van Der Pyl *et al.*, *J. Antibiot.* **45**, 1802-1805 (1992)
2. R. Weindling, *Phytopathol.* **22**, 837-845 (1932)
3. T. Korzybski *et al.*, In “Antibiotics-Origin, Nature and Properties” pp. 1919-1923, American Society for Microbiology (1978)
4. W. A. Rightsel *et al.*, *Nature* **204**, 1333-1334 (1964)
5. P. Waring *et al.*, *Med. Res. Rev.* **8**, 499-524 (1988)
6. M. Okamoto *et al.*, *Chem. Pharm. Bull.* **34**, 340-344 (1986)
7. [937] S. Iwasaki & S. Ōmura, *J. Antibiot.* **60**, 1-12 (2007)
8. T. Fukuyama & Y. Kishi, *J. Am. Chem. Soc.* **98**, 6723-6724 (1976)
9. T. Fukuyama *et al.*, *Tetrahedron* **37**, 2045-2078 (1981)
10. K. C. Nicolaou *et al.*, *J. Am. Chem. Soc.* **134**, 17320-17332 (2012)