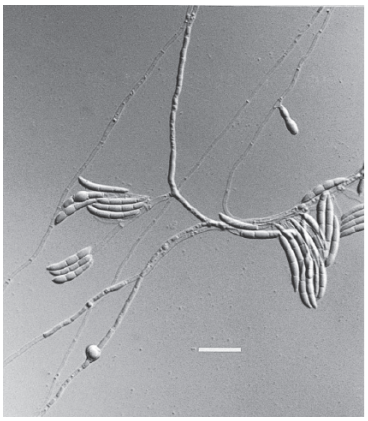
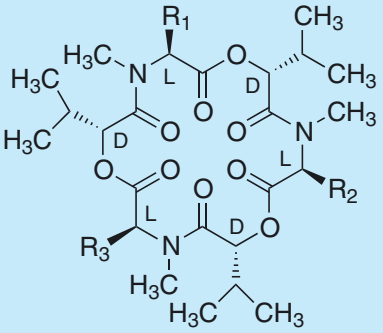
Enniatin

1. Discovery, producing organism and structures[1)]

Enniatins D, E1, E2, and F were isolated from the culture broth of the fungal strain FO-1305 and recognized as inhibitors of acyl-CoA: cholesterol acyltransferase (ACAT) activity by means of an enzyme assay using rat liver microsomes.

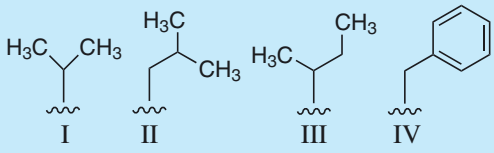


Fusarium sp. FO-1305
Bar: 20 μm



Enniatins

Compound	R_1	R_2	R_3
Enniatin D	I	I	II
Enniatin E1	I	II	III
Enniatin E2	I	III	II
Enniatin F	II	III	III
Enniatin A[2,3)]	III	III	III
Enniatin A1[2,3)]	I	III	III
Enniatin B[2,3)]	I	I	I
Enniatin B1[2,3)]	I	I	III
Beauvericin[4)]	IV	IV	IV



I II III IV

2. Physical data (Enniatin D)

White powder. $C_{34}H_{59}N_3O_9$; mol wt 653.42. Sol. in $CHCl_3$. Insol. in H_2O, hexane.

3. Biological activity[5)]

ACAT inhibition

ACAT inhibitory activity (See also "Purpactin") was tested in an enzyme assay using rat liver microsomes and in a cell assay using J774 macrophages. Cytotoxicity (CD_{50}) was also determined in the cell assay. Enniatins demonstrated amplified ACAT inhibition as the hydrophobicity of the side chain increased, suggesting a relationship between hydrophobicity and ACAT inhibition. Contrastingly, beauvericin having the lowest hydorophobicity, exhibited the most potent ACAT inhibition in the enzyme assay and the best specificity for ACAT inhibition in the cell assay.

Cyclodepsipeptide	Hydrophobicity Retention time (min)*	Rat (liver) microsomes	J774 macrophages		
		IC_{50} (μM)	IC_{50} (μM)	CD_{50} (μM)	CD_{50}/IC_{50}
Enniatin B	8.7	113	0.81	> 10.0	> 12.0
D	10.0	87	0.70	8.0	11.0
B1	10.8	73	0.44	> 5.0	> 11.0
E1/E2	12.5	57	0.28	2.7	9.6
A1	13.6	49	1.10	2.6	2.3
F	15.7	40	0.43	2.9	6.7
A	17.5	22	0.44	2.6	5.9
Beauvericin	12.0	3	0.17	11.0	65.0

* Retention time when eluted through an ODS column (Chemosorb 5ODS-UH, 4.6 x 150 mm; 75% aq. CH_3CN; 1.0 ml/min)

4. References

1. [485] H. Tomoda *et al*., *J. Antibiot*. **45**, 1207-1215 (1992)
2. T. K. Audhya & D. W. Russell, *J. Gen. Microbiol*. **82**, 181-190 (1974)
3. B. D. Doel *et al*., *Aust. J. Chem*. **31**, 1397-1399 (1978)
4. R. L. Hamill *et al*., *Tetrahedron Lett*. 4255-4258 (1969)
5. [491] H. Tomoda *et al*., *J. Antibiot*. **45**, 1626-1632 (1992)