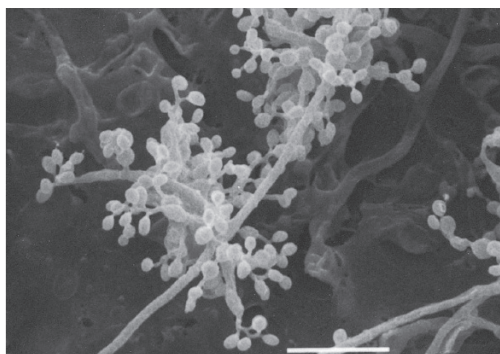


Beauveriolide

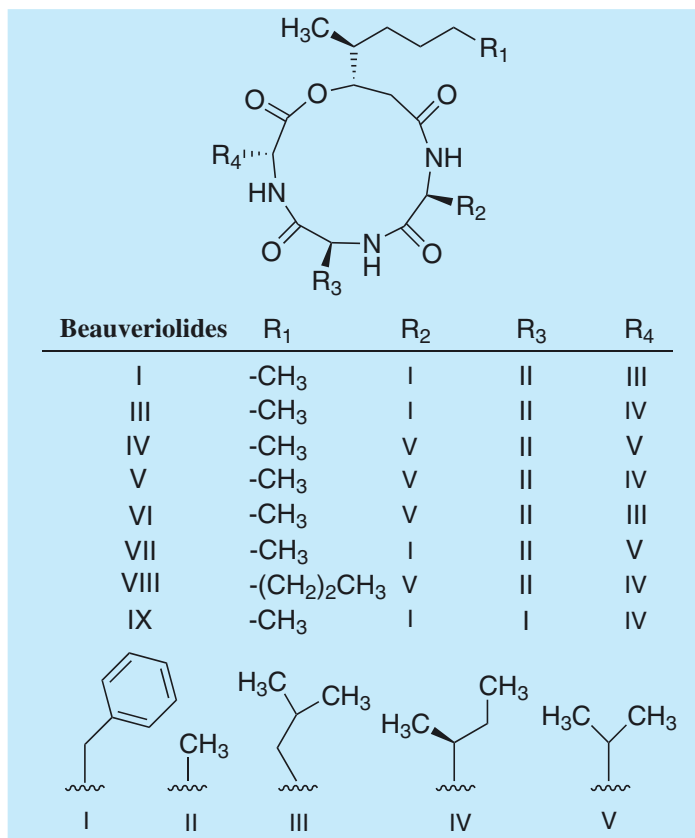
1. Discovery, producing organism and structures^{1-5,10)}

Beauveriolides I¹⁻³⁾, III^{2,3)}, IV, V, VI, VII, VIII and IX⁵⁾ (beauveroplide Fa⁴⁾) were isolated from the culture broth of the fungal strain *Beauveria* sp. FO-6979 and identified by means of an intact cell assay as inhibitors of macrophage foam cell formation. Beauveriolides have a cyclodepsi-peptide structure consisting of three amino acids and a β -hydroxylic acid. Beauveriolide I has been reported as an insecticidal agent¹⁾, beauveriolide IX was identified as beauveriolide Fa⁴⁾, and the planar structure of beauveriolide VI was identical with that of beauveriolide M⁵⁾.



Beauveria sp. FO-6979

Bar: 10 μm



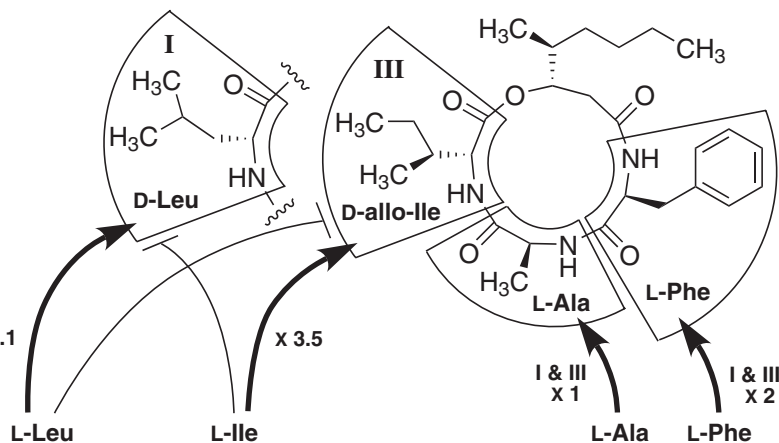
2. Physical data (Beauveriolide III)³⁾

White powder. C₂₇H₄₁N₃O₅; mol wt 487.30. Sol. in MeOH, EtOH, acetone, CH₃CN, EtOAc, CHCl₃. Insol. in H₂O, hexane.

3. Fermentation⁶⁾

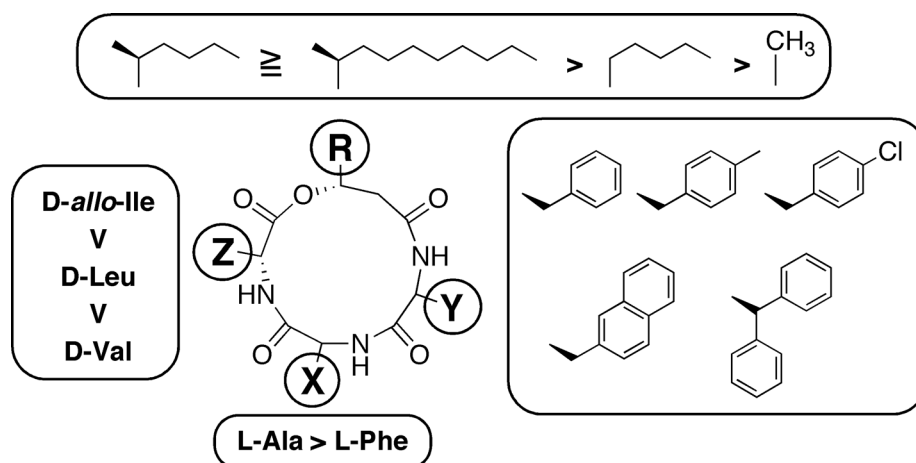
Addition of L-Leu or L-Ile, but not D-Leu or D-allo-Ile, to the culture medium yielded high and selective production of beauveriolide I or III.

Condition	Production ($\mu\text{g}/\text{mL}$)	
	Beauveriolide I	III
Control	25.0	50.0
+ L-Ile	5.6	172.0
+ D-Ile	25.0	50.0
+ L-allo-Ile	24.0	42.0
+ D-allo-Ile	14.0	33.0
+ L-Leu	127.0	26.0
+ D-Leu	24.0	48.0
+ L-Phe	66.0	79.0
+ L-Ala	15.4	26.6
+ L-Val	6.8	7.9



4. Structure-activity relationship^{8,9,11)}

Comparison of ACAT inhibitory activity among natural beauveriolides and synthetic derivatives^{8,9,10)} revealed the structure-activity relationship.

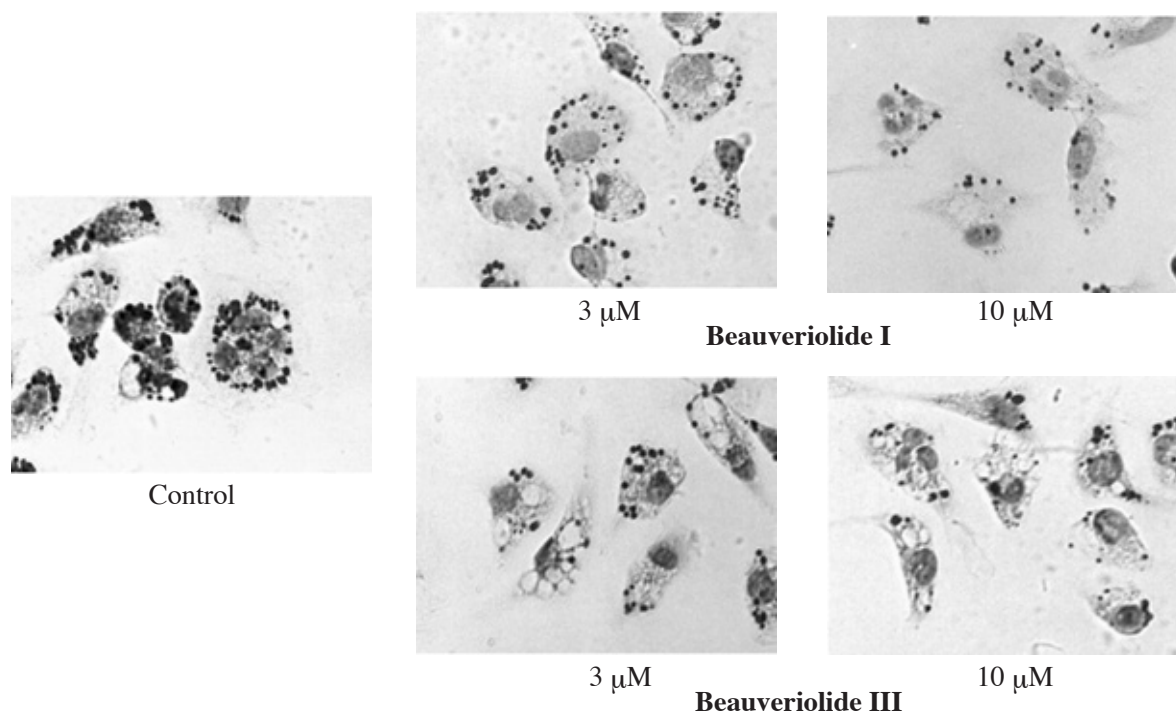


5. Biological activity^{2,12-14)}

Inhibition of lipid droplet formation in mouse peritoneal macrophages.

In the early stages of atherosclerosis, macrophages that penetrate into the intima accumulate massive lipid droplets in the cytosols, and are converted into foam cells, leading to the development of atherosclerosis in the arterial wall. Therefore, inhibitors of macrophage lipid droplet formation would be expected to retard progression of atherosclerosis.

Inhibitory activity against lipid droplet formation in macrophages was tested in a cell assay using mouse peritoneal macrophages. Beauveriolides I and III led to a reduction in the number and size of cytosolic lipid droplets in macrophages at 15 μ M without any cytotoxic effect on the macrophages.



6. References

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