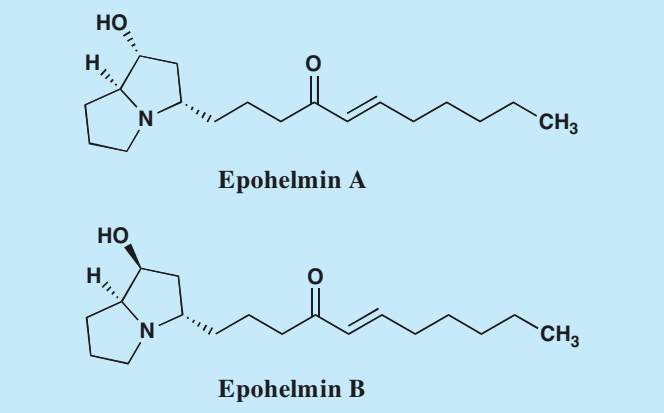
Epohelmin

1. Discovery, producing organism and structures[1,2)]

Epohelmins A and B were isolated from the culture broth of the fungal strain FKI-0929 as lanosterol synthase inhibitors. The structures were revised as 1α-hydroxy-3α-(4'-oxoundec-(*5'E*)-enyl)- pyrrolizidine and 1β-hydroxy-3α-(4'-oxoundec-(*5'E*)-enyl)-pyrrolizidine, respectively, by comparison with the spectral data of synthetic compounds[3)].



Epohelmin A

Epohelmin B

2. Physical data (Epohelmin A)

Colorless oil. $C_{18}H_{31}O_2N$; mol wt 293.44.

3. Biological activity[1)]

3-Hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase is a clinically validated target for suppressing cholesterol biosynthesis. But inhibition of HMG-CoA reductase may cause a simultaneous reduction in the physiologically essential non-sterol isoprenoid metabolites, because it is located upstream in the cholesterol biosynthetic pathway. Therefore, lanosterol synthase (EC 5.4.99.7) is expected to be a more ideal target of inhibition for the development of cholesterol-lowering agents. Epohelmins A and B inhibit recombinant human lanosterol synthase activity with IC_{50} values of 10 and 6.0 μM, respectively.

4. References

1. [873] Y. Sakano *et al*., *J. Antibiot*. **57**, 564-568 (2004)
2. [894] M. Shibuya *et al*., *J. Antibiot*. **58**, 599-601 (2005)
3. B. B. Snider *et al*., *Org. Lett*. **7**, 4419-4422 (2005)