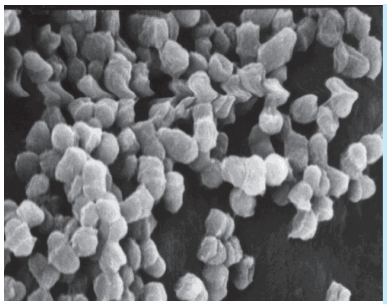
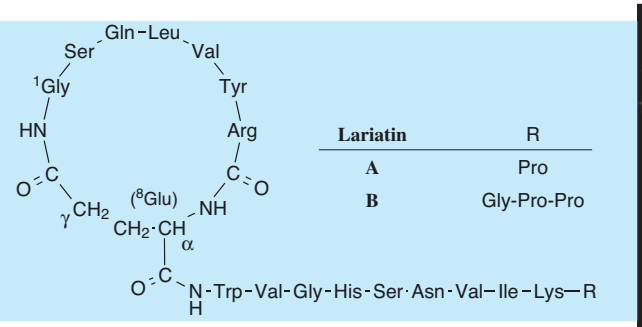
Lariatin

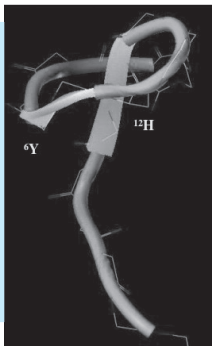
1. Discovery, producing organism and structures[1,2)]

Lariatins were isolated from the culture broth of the Gram-positve *Rhodococcus jostii* strain K01-B0171 as selective antimycobacterial agents. The strain K01-B171 was isolated from the inside of soil aggregates. Lariatins are unique cyclic peptides consisting of 18 and 20 L-amino acid residues with an internal linkage between the γ-carboxyl group of Glu8 and the α-amino group of Gly1. The three-dimensional structure of lariatin A deduced from NMR data indicates that the tail segment (Trp9-Pro18) passes through the ring segment (Gly1-Glu8) to form a 'lasso' structure.



Rhodococcus jostii
K01-B0171





Lasso structure of
lariatin A

2. Physical data (Lariatin A)

Yellow powder. $C_{94}H_{144}N_{27}O_{25}$; mol wt 2051.31. Sol. in H_2O, DMSO, MeOH. Insol. in $CHCl_3$.

3. Biological activity[1,3)]

1) Antimycobacterial activity[1,3)]

Lariatin A exhibits the growth of *Mycobacterium tuberculosis* with an MIC of 0.39 μg/ml in liquid microdilution method.

2) Antimicrobial activity[1)]

Lariatins exhibit selective activity against *Mycobacterium smegmatis*.

Test organism	Inhibition zone (mm) at 10 μg/6 mmdisk		
	Lariatin A	Lariatin B	Isoniazid
Staphylococcus aureus ATCC6538P	–	–	–
Bacillus subtilis ATCC6633	–	–	–
Micrococcus luteus ATCC9341	–	–	–
Mycobacterium smegmatis ATCC607	19	18	26
Esherichia coli NIHJ	–	–	–
Pseudomonas aeruginosa IFO3080	–	–	–
Xanthomonas campestris KB88	–	–	–
Acholeplasma laidlawii KB174	–	–	–
Pyricularia oryzae KB180	–	–	–
Aspergillus niger ATCC9642	–	–	–
Mucor racemosus IFO4581	–	–	–
Candida albicans ATCC645648	–	–	–
Saccharomyces cerevisiae KF26	–	–	–

4. Biosynthesis[4)]

The biosynthetic gene cluster for lariatin was identified and the biosynthetic pathway was proposed as follows. The linear precursor peptide is synthesized ribosomally, followed cleavage by peptidase and formation of amide bond between gylcine and glutamic acid.

5. References

1. [957] M. Iwatsuki *et al*., *J*. *Antibiot*. **60**, 357-363 (2007)
2. [911] M. Iwatsuki *et al*., *J*. *Am*. *Chem*. *Soc*. **128**, 7486-7491 (2006)
3. [1054] M. Iwatsuki *et al*., *Bioorg*. *Med*. *Chem*. *Lett*. **19**, 2888-2890 (2009)
4. J. Inokoshi *et al*., *Appl*. *Microbiol*. *Biotechnol*. 95, 451-460 (2012)