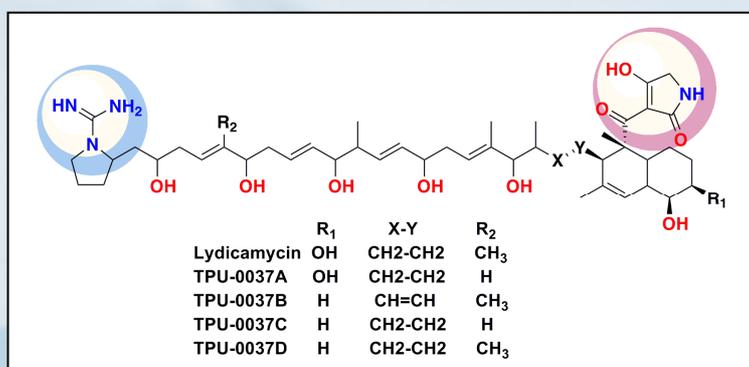


## Lydicamycins

### Novel Antibiotic Scaffold

In 1991, researchers at University of Toyko discovered a structurally novel antibiotic from *Streptomyces lydicus* and named the metabolite **lydicamycin**. Unlike many of the known antibiotic classes from *Streptomyces*, **lydicamycin** is not a macrocyclic lactone but rather a straight chain terminating at one end with a decalin bearing a tetramic acid and the other end bearing a basic amidinopyrrolidino moiety. **Lydicamycin** was selectively active against G+ve bacteria showing excellent activity against MRSA.



Almost 10 years later researchers at Toyama Perfectural University in Japan isolated **lydicamycin** as part of a complex of related analogues designated Antibiotic **TPU-0037A to D** isolated from *S. platensis*. Together the metabolites complete the set of known members of the **lydicamycin** class. Unusually in microbial metabolites, the class shows very limited structural variation at C<sub>8</sub> (R<sub>1</sub>), C<sub>30</sub> (R<sub>2</sub>) and unsaturation at C<sub>14</sub>-C<sub>15</sub> (X...Y). Whether this lack of structural diversity reflects the rare occurrence of **lydicamycin** in nature and more are yet to be discovered, or reflects the restraints imposed by their respective mode of action is unknown. Like **lydicamycin**, the TPUs are G+ve selective and active against MRSA strains.

Curiously, a truncated **lydicamycin** bearing the decalin tetramic acid moiety, Antibiotic BU-4514N, was isolated from *Micromonospora* sp.. While the metabolite was shown to possess weak antibiotic activity it was shown to have powerful neuritogenic activity. Limited access to the **lydicamycins** has restricted a more thorough investigation of their pharmacology.

#### Rare Microbes

Producers of **lydicamycin** are very rare with only 5 examples in our collection, occurring with an incidence of ~1

in 100,000 cultures. At BioAustralis we isolate **lydicamycin** from *Streptomyces* sp. MST-66492, an unidentified *Streptomyces* sp. culture isolated from land by Lake Bolac in South Australia and the TPUs are isolated from *Streptomyces* sp. MST-112218 isolated from swampy soil near Kingscote, also in South Australia.

#### The Opportunities

The mode of action, selectivity of more modern resistant strains, analogue synthesis and structure-activity relationships, and interaction with other classes of antibiotics have never been investigated. An unusual structural scaffold deserving of more attention.

1. Lydicamycin, a new antibiotic of a novel skeletal type. I. Taxonomy, fermentation, isolation and biological activity. Hayakawa Y. et al. *J. Antibiot.* **1991**, 44, 282.
2. Lydicamycin, a new antibiotic of a novel skeletal type. II. Physico-chemical properties and structure elucidation. Hayakawa Y. et al. *J. Antibiot.* **1991**, 44, 288.
3. TPU-0037-A, B, C and D, novel lydicamycin congeners with anti-MRSA activity from *Streptomyces platensis* TP-A0598. Furumai T. et al. *J. Antibiot.* **2002**, 55, 873.
4. A new neuritogenic compound BU-4514N produced by *Microtetraspora* sp.. Toda S. et al. *J. Antibiot.* **1993**, 46, 875.

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