# CHAPTER II

## REVIEW OF LITERATURE

The natural habitats of microorganisms are exceedingly diverse (Brock and Madigan, 1988). In many cases, we have found that the chemicals produced by these microorganisms exhibit various biological activities especially antibacterial and antifungal activities. Most of antibiotics were produced from actinomycetes especially soil actinomycetes (Jensen and Fenical, 1994). Although many antibiotics have been developed in the last few decades (Tortora, Funke, and Case, 1982), relatively few are used in chemotherapy. This is because many antibiotics damage normal cells in concentrations needed to kill pathogenic microorganisms. At present, drug resistance of bacteria and widespread of human immunodeficiency viruses are increasing, so researchers have been trying to find new antibiotics to control these problems (Service, 1995). Many scientists hope that novel antibiotics will be discovered in new or unusual microorganisms isolated from the marine ecosystems, which are quite different from terrestrial ones (Okami, 1986).

### 1. Characterization of gram-positive endospore-forming rods, *Bacillus*

The bacterial isolation is one of the most important part of new drug discovery. It is convenient to divide bacteria into two major groups, gram-positive and gram-negative bacteria, based on the reactions of the microorganisms to gram's method of staining (Barrow and Feltham, 1993). The gram-positive endospore-forming rods are the genera *Bacillus* and *Clostridium*. *Bacillus* species are aerobes, whereas *clostridium*

species are obligate anaerobes (Barrow and Feltham, 1993). Several species of the genus *Bacillus* produce antibiotics, while many species of the genus *Clostridium* produce toxins.

The endospore-forming bacteria, most of which are gram-positive motile rods, a diverse assemblage that is a grouping of convenience. At present it can be grouped the aerobic, anaerobic and facultative endospore-forming rods into eight genera, *Paenibacillus*, *Bacillus*, *Sporolactobacillus*, *Amphibacillus*, *Halobacillus*, *Brevibacillus*, *Aneurinibacillus*, and *Alicyclobacillus* (Shida *et al.*, 1997). The morphology, physiology, biochemical reactions, and G+C content of the genera of endospore-forming rods are summarized in Table 1.

With recent descriptions of numerous new members, the genus *Bacillus* has become unwieldly though many of the species can still be identified by conventional tests (Barrow and Feltham, 1993). An identification table (Table 2) has been used to identify the *Bacillus* species (Barrow and Feltham, 1993).

Bacteria in the genus *Bacillus* are cells, rod-shaped, straight or nearly straight; endospores, very resistant to many diverse conditions; sporulation not repressed by exposure to air; gram-positive, or positive only in early stages of growth, or negative; flagella, peritrichous or degenerately peritrichous; aerobic or facultatively anaerobic; colony morphology and size very variable; pigments may be produced on certain media; exhibit a wide diversity of physiological ability; and some strains are salt tolerant, others have specific requirements for salts. Catalase is formed by most species; oxidase-positive or negative. The cell wall peptidoglycan of most species belongs to the directly cross-linked *meso*-diaminopimelic acid type. The G+C content of the DNA is 32-69 mol%.

Aerobic endospore-forming bacteria of the genus *Bacillus* can be isolated from almost all natural habitats and from many other sources. They are most commonly found in soil and in plant litter where they play an important role in the biological cycling of carbon and nitrogen. Other habitats like freshwater, polluted seawater, deep-sea sediments, foods, milk, pharmaceuticals, may have acquired these organisms from soil by runoff, from dust, from infected plant materials. Such habitats may provide conditions suitable for the growth of *Bacillus* strains or may only harbor spores which, due to their remarkable power of resistance and dormancy, may survive in any habitat for long periods (Berkeley and Claus 1986). Thus, it is generally not possible to draw any conclusion from the site of isolation of a *Bacillus* strain as to its real natural habitat, although they are a few exceptions to this generation.

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**Table 1.** Characteristics of the genera of aerobic, anaerobic and facultative endospore-forming rods

| Characteristics[a] | *Paenibacillus* | *Bacillus* | *Sporolactobacillus* | *Amphibacillus* | *Halobacillus* | *Brevibacillus* | *Aneurinibacillus* | *Alicyclobacillus* |
|---|---|---|---|---|---|---|---|---|
| cell shape | rod | rod | rod | rod | rod or spherical to oval | | | |
| spore shape | oval | oval or spherical | oval | oval | oval | oval | oval | oval |
| sporangia | swollen | swollen or not swollen | swollen | swollen | swollen | swollen | swollen | swollen or not swollen |
| anaerobic growth | v | v | + | + | - | - | - | - |
| catalase | v | + | - | - | + | + | + | + |
| hydrolysis of thiamine | NT | NT | NT | NT | NT | - | + | NT |
| production of lactic acid | NT | v | + | + | NT | NT | NT | NT |
| Voges-Proskauer test | v | v | NT | NT | - | - | - | v |
| pH in Voges-Proskauer broth | <6.0 | v | NT | NT | NT | >7.0 | >7.0 | NT |
| growth in the presence of 10% NaCl | - | v | - | - | + | - | - | - |
| optimum growth conditions | | | | | | | | |
| pH | 7.0 | v (7.0-9.5) | 7.0 | 9.0 | 7.5 | 7.0 | 7.0 | 3.0 |
| temperature (°C) | 23-37 | v (15-55) | 30 | 37 | 35 | 30-48 | 37 | 65 |
| G+C content (mol%) | 39-54 | 32-69 | 39 | 36-38 | 40-43 | 46-57 | 42-43 | 52-60 |

[a]Data from Shida *et al.*,1997.

-, Negative reaction; +, Positive reaction; NT, Not tested; v, Variable reaction.

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**Table 2.** Characteristics of *Bacillus* species

| Characteristics[a] | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| gram reaction | + | + | + | + | d | + | + | + | + | + | + | d | d | d | - | d | + | - | - | d | + | d | d | d |
| chains of cells | + | + | + | + | d | d | + | + | d | d | d | d | d | d | - | d | - | - | - | - | + | d | - | d |
| motility* | - | + | - | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| cell length > 3 μm | + | + | + | + | - | - | d | - | - | - | - | + | - | + | d | d | d | d | d | + | + | - | - | - |
| spore position and shape | vx | vx | vx | vx | vx | vx | vx | vx | vx | vx | vx | vtx | tyx | vx | vx | vtx | vx | vx | vx | ty | vtx | vx | vx | vtx |
| swelling of cell body by spore | - | - | - | - | d | d | - | - | - | - | - | d | + | + | + | + | + | + | + | + | - | d | + | + |
| growth at 50°C | - | - | - | - | - | - | - | d | + | + | + | + | + | - | + | d | - | + | - | - | d | + | + | + |
| growth in 10% NaCl | + | d | d | d | + | - | - | + | d | - | + | - | + | - | - | - | - | - | - | - | - | - | - | - |
| anaerobic growth | + | + | + | + | - | - | - | - | - | + | - | + | + | + | - | + | + | + | + | - | - | d | - | - |
| carbohydrates, acid from | | | | | | | | | | | | | | | | | | | | | | | | |
| glucose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | - | + | + | + | + | - | - | + | + | + |
| cellobiose | - | d | d | d | - | d | + | + | + | + | + | d | - | + | - | + | d | + | + | - | - | d | d | d |
| galactose | - | - | d | - | - | d | + | + | d | + | d | d | - | d | - | + | - | + | + | - | - | - | - | - |
| mannose | - | - | - | d | d | + | d | + | + | + | d | + | d | d | - | + | d | + | + | - | - | + | d | + |
| melibiose | - | - | - | - | - | d | + | d | d | d | d | + | - | d | - | + | - | + | + | - | - | d | - | + |
| raffinose | - | - | - | - | - | - | d | + | + | d | + | + | - | + | - | + | - | + | + | - | - | d | d | + |
| salicin | - | + | d | d | - | d | + | + | + | + | + | d | d | d | - | + | d | + | + | - | - | d | + | d |
| xylose | - | - | - | - | - | - | + | + | d | + | d | d | - | - | - | + | - | + | + | - | - | d | + | - |
| ONPG | - | - | d | - | d | + | + | + | + | + | d | d | d | d | d | + | - | + | + | - | - | d | - | - |
| utilization of citrate | - | d | d | + | - | - | + | + | + | + | d | d | - | - | d | - | - | - | d | d | - | - | - | - |

**Table 2.** Characteristics of *Bacillus* species (continued)

| Characteristics[a] | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| urease | - | d | d | - | - | + | d | - | - | d | - | - | - | d | - | - | - | - | - | d | - | - | - | - |
| indole | - | - | - | - | - | - | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - |
| Voges-Proskauer test | + | + | + | + | - | - | - | + | + | d | + | d | d | + | - | d | + | d | + | - | - | d | + | d |
| nitrate reduction | + | + | + | + | + | - | d | - | + | + | + | d | d | - | d | d | + | + | + | d | - | + | - | d |
| hydrolysis of : | | | | | | | | | | | | | | | | | | | | | | | | |
| casein | + | + | + | + | + | - | + | + | + | + | + | + | + | + | + | - | d | - | + | + | d | - | - | d |
| hippurate | - | - | - | - | + | + | - | + | d | - | - | + | - | + | + | - | d | d | - | - | d | + | + | + |
| starch | + | + | + | + | + | + | + | - | + | + | + | + | - | + | - | + | - | + | + | - | - | +- | - | + |
| oxidase | d | d | d | d | - | + | - | - | - | - | - | - | d | + | - | - | - | + | - | + | d | - | - | - |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | *B. anthracis* | 5 | *B. firmus* | 9 | *B. subtilis* | 13 | *B. pantothenticus* | 17 | *B. laterosporus* | 21 | *B. badius* | |
| 2 | *B. cereus* | 6 | *B. lentus* | 10 | *B. licheniformis* | 14 | *B. alvei* | 18 | *B. macerans* | 22 | *B. stearothermophilus* (Group I) | |
| 3 | *B. mycoides* | 7 | *B. megaterium* | 11 | *B. amyloliquefaciens* | 15 | *B. brevis* | 19 | *B. polymyxa* | 23 | *B. stearothermophilus* (Group II) | |
| 4 | *B. thuringiensis* | 8 | *B. pumilus* | 12 | *B. coagulans* | 16 | *B. circulans* | 20 | *B. sphaericus* | 24 | *B. stearothermophilus* (Group III) | |

[a]Data from Barrow and Feltham,1993.
*All motile species may produce non-motile variants.
ONPG, *o*-nitrophenyl-β-D-galactopyranoside.
+, 85-100% Strains are positive; d, 16-84% Strains are positive; -, 0-15% Strains are positive;
t, Spore terminal; v, Spore central/subterminal; x, Spore oval (ellipsoidal); y, Spore round.

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**2. Bioactive natural products from *Bacillus***

The function of antibiotics in the producing organisms has been the subject of considerable speculation and discussion. Still under current consideration (Katz and Demain, 1977) is the possibility that antibiotics function to kill or to inhibit the growth of other organisms in nature, thereby providing a competitive advantage to the producing species. A further variation of the competitive hypothesis involves the excretion of the antibiotic during spore germination in order to eliminate competitors in the immediate environment of the germinating spore. An additional hypothesis currently states that synthesis of an antibiotic (or other secondary metabolites) is a method of avoiding cell death due to unbalanced growth. With respect to the unbalanced growth hypotheses, it is assumed that the overproduced primary metabolites can be converted to the antibiotics which are released from the cell. The detoxification hypothesis proposed that certain toxic metabolites can be converted to the antibiotics which are not toxic to the producing organisms. It has been unclear about the function of antibiotics in the producing microorganisms. Whatever the true function of antibiotics, many mechanisms exist whereby organisms can protect themselves from the antibiotics they elaborate. Permeability changes, compartmentalization, and the presence of an inactive form of the antibiotic intracellularly may all play a role in preventing self-annihilation.

Bacteria in the genus *Bacillus* is one of the most important natural resources of antibiotics. A review on the compounds, species, structures, and biological activities of antibiotics obtained by strains of *Bacillus* species is shown in Table 3.

**Table 3.** Antibiotics elaborated by strains of *Bacillus* species.

| Compounds | Strains | Structures | Activities | References |
|---|---|---|---|---|
| 102804 | *B. cereus* 102804 | ND | against gram-positive and gram-negative bacteria | Kageyama, Burg, and Perlman, 1977 |
| 333-25 | *B. circulans* 333-25 | acylpeptide containing 2,4-diamino-butyric acid | against gram-positive and gram-negative bacteria | Shoji *et al.*, 1976 |
| 339-29 | *B. pumilus* 339-29 | peptide | against gram-positive bacteria | Shoji *et al.*, 1976 |
| 61-26 | *Bacillus* sp. 61-26 | peptide | against gram-positive bacteria and fungi | Shoji *et al.*, 1975 |
| ADP-III | *B. subtilis* C756 | acylpeptide | inhibition of cyclic adenosine-3',5'-monophosphate (cAMP) phosphodiesterase | Hosono and Suzuki, 1983 |
| alboleutin | *B. subtilis* AF-8 | ND | ND | Omura *et al.*, 1980 |
| alphostatin | *B. megaterium* BMG 59-R2 | ND | inhibition of alkaline phosphatase | Aoyagi *et al.*, 1989 |
| alvein | *B. alvei* | polypeptide | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| ambutyrosine B | *B. biterinus* | ND | against gram-positive bacteria | Glasby, 1993 |
| amicoumacins A-C | *B. pumilus* BN-103 | ND | against gram-positive bacteria, antiinflammatory, and antiulcer | Itoh *et al.*, 1981 |
| 20-*O*-demethyl ansamitocin, 20-*O*-demethyl ansamitocin P-3, 1,15-hydroxyansamitocin P-3, and N-demethyl ansa-mitocin P-3 | *B. megaterium* IFO 12108 | ansamycin | against tumor cells | Izawa *et al.*, 1981 |
| antibiotic 60-6 | *B. cereus* 60-6 | ND | against gram-positive bacteria | Glasby, 1993 |
| antibiotic 61-26 | unclassified *Bacillus* | ND | against gram-positive bacteria | Glasby, 1993 |
| antibiotic 339-29 | *B. pumilus* | ND | against gram-positive bacteria | Glasby, 1993 |

**Table 3.** Antibiotics elaborated by strains of *Bacillus* species (continued).

| Compounds | Strains | Structures | Activities | References |
|---|---|---|---|---|
| antibiotic 340-19-II | *B. lacterospo-rus* No. 340-19 | ND | against *Klebsiella pneumoniae* and *Staphylococcus aureus* | Glasby, 1993 |
| antibiotics 1316-B1-B3 | *B. subtilis* AJ 1316 | ND | against gram-positive bacteria | Glasby, 1993 |
| antibiotic 1998 | *B. brevis* AS1998 | ND | against gram-positive bacteria | Glasby, 1993 |
| antibiotic 2725 | *B.licheniformis* 2725 | polypeptide | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| antibiotic AI-77B | *B. pumilus* | ND | gastroprotective | Glasby, 1993 |
| antibiotic AR-110 | *B. polymyxa* AR-110 | ND | against gram-positive bacteria | Glasby, 1993 |
| antibiotic B-43 | *B. circulans* | polypeptide | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| antibiotic BN-7 | *B. circulans* BN-7 | polypeptide | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| antibiotic BN-103 | *B. pumilus* BN-103 | ND | against gram-positive bacteria | Glasby, 1993 |
| antibiotic BN-175 | *Bacillus* sp. BN-175 | ND | against gram-positive bacteria and *Candida* species | Glasby, 1993 |
| antibiotic Bu-1880 | *B. circulans* Bu-1880 | polypeptide | against gram-positive bacteria | Glasby, 1993 |
| antibioic Bu-1975-$A_1$ | *B. circulans, B. croceus, B. biotinicus* and *B. proteophilus* | ND | against gram-positive bacteria | Glasby, 1993 |
| antibiotic Bu-1975-$C_1$ | *B. circulans* | ND | against *Escherichia coli* and *Klebsiella pneumoniae* | Glasby, 1993 |
| antibiotic EM-49 | *B. circulans* ATCC 21656 | polypeptide | against a number of bacteria, fungi, and protozoa | Glasby, 1993 |
| antibiotic FR-900493 | *B. cereus* | ND | against *Staphylococcus aureus* | Glasby, 1993 |
| antibiotic G-15 I-II | *B. cereus* G-15 | ND | against gram-positive bacteria | Glasby, 1993 |

**Table 3.** Antibiotics elaborated by strains of *Bacillus* species (continued).

| Compounds | Strains | Structures | Activities | References |
|---|---|---|---|---|
| antibiotic GIF-2 | *B. cereus* | ND | against gram-positive bacteria | Glasby, 1993 |
| antibiotic Gp-3 | *B. cereus* Gp-3 | ND | against gram-positive bacteria | Glasby, 1993 |
| antibiotic KBS3-P1004 | *Bacillus* species | ND | against fungi | Glasby, 1993 |
| antibiotic KM-214 | *B. aurantinus* | ND | against bacteria and fungi | Glasby, 1993 |
| antibiotic MX-A | *B. biterinus* Z-1159, and *B. circulans* V-7 | ND | against *Pseudomonas aeruginosa* | Glasby, 1993 |
| antibiotic P2 | *B. subtilis* 260 | ND | against fungi | Glasby, 1993 |
| antibiotic P4 | *B. subtilis* 060 | ND | against fungi | Glasby, 1993 |
| antibiotic TL-119 | *B. subtilis* | peptide | against gram-positive, gram-negative bacteria, and inhibit enzyme | Glasby, 1993 |
| antibiotic Y-05460M | *Bacillus* sp. Y-05460M | ND | against *Flavobacterium* 633, *K. pneumoniae*, and *S. aureus* | Glasby, 1993 |
| antibiotic Y-8495 | *B. bungoensis* | peptide | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| N-5-hydroxy-L-arginine | *Bacillus* sp. XB-13248 | modified amino acid | against bacteria | Maehr *et al.*, 1973 |
| aurantinin B | *B. aurantinus* | ND | against bacteria | Konda *et al.*, 1988 |
| aurantinin (KM-214) | *B. aurantinus* | conjugated triene | against gram-positive bacteria | Nishikiori *et al.*, 1978 |
| ayfivin | *B. licheniformis* | peptide | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| azoxybacillin | *B. cereus* NR 2991 | ND | against fungi | Fujiu *et al.*, 1994 |
| B-43 | *B. circulans* B-43 | peptide | against gram-positive and gram-negative bacteria | Shoji *et al.*, 1976 |
| bacillin | *B. subtilis* No. KM-208 | ND | against gram-positive and gram-negative bacteria | Glasby, 1993 Atsumi, Oiwa, and Omura, 1975 |

**Table 3.** Antibiotics elaborated by strains of *Bacillus* species (continued).

| Compounds | Strains | Structures | Activities | References |
|---|---|---|---|---|
| bacillipin A | *B. subtilis* | ND | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| bacillomycin B | *B. subtilis* AF 1 | polypeptide | against fungi | Glasby, 1993 |
| bacillomycin C | *B. subtilis* AF 2 | polypeptide | against fungi | Glasby, 1993 |
| bacillomycins Fb-Fc | *B. subtilis* I-164 | cyclic lipopeptides | against fungi | Besson and Michel, 1988 |
| bacillomycin Lc | *B.subtilis* FS94-14 | cyclic lipopeptide | against fungi | Eshita *et al.*, 1995 |
| bacillopeptins A-C | *B. subtilis* FR-2 | cyclic lipopeptide | against fungi | Kajimura, Sugiyama, and Kaneda, 1995 |
| bacillomycin D | *B. subtilis* | cyclic lipopeptide | against fungi | Peypoux *et al.*, 1980 |
| bacillomycin F | *B. subtilis* I-164 | cyclic lipopeptide | against fungi | Mhammedi *et al.*, 1981 |
| bacilysin | *B. subtilis* | peptide | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| bacimethrin | *B. megaterium* | ND | against gram-positive bacteria | Glasby, 1993 |
| baciphelacin | *B. thiaminolyticus* IFO 3967/B-1-7 | ND | against bacteria and leukemic cells | Okazaki *et al.*, 1975 |
| bacithrocins A-C | *B. lacterosporus* Laubach NR 2988 | N-acyl-L-phenylalanyl-DL-arginals | inhibit thrombin | Kamiyama *et al.*, 1994 |
| bacitracin A-G | *B.licheniformis* and *B. subtilis* | polypeptides | against gram-positive and gram-negative bacteria | Ikai *et al.*, 1995 |
| bagougera-mines A-B | *B. circulans* TB-2125 | nucleosides | against bacteria and spotted spider mite | Takahashi *et al.*, 1986 |
| biocerin | *B. cereus* | ND | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| BMY-28160 | *B. circulans* H 913-B4 | peptide | against fungi | Sugawara, Konishi, and Kawaguchi, 1984 |
| bresseine | *B. brevis* | peptide | against bacteria | Katz and Demain, 1977 |
| brevin | *B. brevis* | peptide | against bacteria | Katz and Demain, 1977 |

**Table 3.** Antibiotics elaborated by strains of *Bacillus* species (continued).

| Compounds | Strains | Structures | Activities | References |
|---|---|---|---|---|
| brevistin | *B. brevis* 342-14 | peptide | against gram-positive bacteria | Shoji *et al.*, 1976 |
| BU-1709E1-E2 | *B. circulans* YQW-B6 | aminoglyco-sides | against bacteria | Tsukiura *et al.*, 1973 |
| BU-2470 A, B1, B2a, and B2b | *B. circulans* Bu-2470 | octapeptides | against bacteria | Sugawara *et al.*, 1983 Konishi *et al.*, 1983 |
| BU-2743E | *B. circulans* J725-B93 | ND | inhibition of leucine aminopeptidase | Kobaru *et al.*, 1983 |
| butirosin B | *B. circulans* | ND | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| 2-hydroxy-butirosin | *B. circulans* deoxystrepta-mine-lacking mutant | ND | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| 6'-deamino-6'-hydroxy butirosin and 3',4'-dideoxy-6'-C-methyl butirosin B | *B. circulans* MCRL 5003 | ND | against bacteria | Takeda *et al.*, 1978 |
| 4'-deoxybuti-rosin A-B | *B. circulans* No. C. 308-B4 | aminoglyco-sides | against bacteria | Kawaguchi *et al.*, 1974 |
| butirocin derivatives | *B. circulans* mutant | ND | against bacteria | Taylor and Schmitz, 1976 |
| cerexins A-B | *B. cereus* Gp-3 | peptides | against gram-positive bacteria | Shoji *et al.*, 1975 |
| cerexins C-D | *B. cereus* Gp-3 | peptides | against bacteria | Shoji *et al.*, 1976 |
| circulin | *B. circulans* | peptide | against bacteria | Katz and Demain, 1977 |
| cispentacin | *B. cereus* L450-B2 | ND | against fungi | Konishi *et al.*, 1989 |
| colistins pro-A-C | *B. polymyxa* subsp. *colistinus* | ND | against bacteria | Kimura, Kitamura, and Hayashi, 1982 |
| difficidin | *B. subtilis* MB 3575 | polyene macrolide | against gram-positive bacteria | Glasby, 1993 |
| diprotins A-B | *B. cereus* BMF 673-RF1 | ND | inhibition of dipeptidyl aminopeptidase IV | Umezawa *et al.*, 1984 |

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**Table 3.** Antibiotics elaborated by strains of *Bacillus* species (continued).

| Compounds | Strains | Structures | Activities | References |
|---|---|---|---|---|
| edeine A1 | *B. brevis* Vm4 | peptide | reversibly binding to polynucleotides *in vitro*, and inhibition of DNA and protein synthesis *in vivo* | Glasby, 1993 |
| edeine B1 | *B. brevis* Vm4 and mutant 587 | ND | reversibly binding to polynucleotides *in vitro*, and inhibition DNA and protein synthesis *in vivo* | Glasby, 1993 |
| EM-49 | *B. circulans* ATCC 21656 | peptide | against parasites | Katz and Demain, 1977 Mayers *et al.*, 1973 |
| endosubtylisin | *B. subtilis* | ND | against gram-negative bacteria | Glasby, 1993 |
| eseine | *B. brevis* | peptide | against bacteria | Katz and Demain, 1977 |
| esperine | *B. mesenteri-cus* | peptide | against gram-positive bacteria | Glasby, 1993 |
| eumycin | *B. subtilis* | ND | against fungi | Glasby, 1993 |
| fengycin | *B. subtilis* F 29-3 | lipopeptide | against filamentous fungi | Vanittanakom *et al.*, 1986 |
| fenycin | *B. subtilis* | lipopeptide | ND | Taraz *et al.*, 1999 |
| fluvomycin | *B. subtilis* | ND | against bacteria and fungi | Glasby, 1993 |
| FR 901537 | *Bacillus* sp. 3072 | pathetheine naphthol derivative | aromatase inhibitor | Oohata *et al.*, 1995 |
| fusaricidin A | *B. polymyxa* KT-8 | depsipeptide | against gram-positive bacteria and fungi | Kajimura and Kaneda, 1996 |
| fusaricidins B-C | *B. polymyxa* KT-8 | depsipeptides | against gram-positive bacteria and fungi | Kajimura and Kaneda, 1997 |
| galantins I-II | *B. pulvifaciens* 52-33 | peptides | against gram-positive, acid-fast, and gram-negative bacteria | Shoji *et al.*, 1975 |
| gatavalin | *B. polymyxa* subsp. *colistinus* | peptide | against fungi | Nakajima *et al.*, 1972 |

**Table 3.** Antibiotics elaborated by strains of *Bacillus* species (continued).

| Compounds | Strains | Structures | Activities | References |
|---|---|---|---|---|
| 3-amino-3-deoxy-D-glucose | *B. aminoglycosidicus* A-4722 | ND | against bacteria | Umezawa *et al.*, 1967 |
| glysperins A-C | *B. cereus* F173-B61 | ND | against gram-positive and gram-negative bacteria | Kawaguchi *et al.*, 1981 |
| gramicidin S | *B. brevis* | peptide | against bacteria | Katz and Demain, 1977 |
| gramicidins S2-S3 | *B. brevis* | ND | against bacteria | Nozaki and Marumatsu, 1984 |
| 4-keto-5-amino-6-hydroxy-hexanoic acid | *B. cereus* 102804 | ND | against gram-positive and gram-negative bacteria | Perlman *et al.*, 1981 |
| isohalobacillin | *Bacillus* sp. A1238 | complex of cyclic acyl-peptide | Inhibition of acyl-CoA : cholesterol acyltransferase | Hasumi *et al.*, 1995 |
| iturin AL | *B. subtilis* A114 | cyclic lipopeptide | against fungi | Winkelmann *et al.*, 1983 |
| iturins C2-C4 | *Bacillus* sp. A 2822 | cyclic lipopeptides | inhibitors of oxidized low density lipoprotein (LDL) binding | Park, Hasumi, and Endo, 1995 |
| iturins D-E | *B. subtilis* | cyclic lipopeptides | against fungi | Besson and Michel, 1987 |
| jolipeptin | *B. polymyxa* subsp. *colistinus* ATCC 21830 | peptide | against gram-positive and gram-negative bacteria | Ito and Koyama, 1972 |
| KM-214 | *B. aurantinus* KM-214 | ND | against bacteria | Omura *et al.*, 1976 |
| lacterospora-mine | *B. lacterosporus* | non-peptide | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| lacterosporin A | *B. lacterospous* | ND | against *Mycobacterium phlei* and *S. aureus* | Glasby, 1993 |
| lakacidin C | *B. megaterium* IFO 12108 | lankacidin | inhibition of tumor cell growth | Nakahama, Harada, and Igarasi, 1975 |
| laterospora-mine | *B. lacterosporus* 340-19 | non-peptidic structure | against gram-positive and gram-negative bacteria | Shoji *et al.*, 1976 |
| leuhistin | *B. laterosporus* BMI 156-14F1 | ND | inhibition of aminopeptidase M | Aoyagi *et al.*, 1991 |

**Table 3.** Antibiotics elaborated by strains of *Bacillus* species (continued).

| Compounds | Strains | Structures | Activities | References |
|---|---|---|---|---|
| licheniformin | *B. licheniformis* | ND | against *M. phlei* and *S. aureus* | Glasby, 1993 |
| mersacidin | *Bacillus* sp. HIL Y-85, 54728 | peptide containing beta-methyl-lanthionine | against gram-positive bacteria | Chatterjee *et al.*, 1992 |
| mycobacillin | *B. subtilis* | peptide | against fungi | Katz and Demain, 1977 |
| micrococcin P | *B. pumilus* | peptide | against bacteria | Katz and Demain, 1977 |
| hydroxymycotrienins A-B | *Bacillus* sp. BMJ 958-62F4 | ansamycin | inhibition of tumor cell growth | Hosokawa *et al.*, 1996 |
| 34-hydroxy-mycotrienin-II and 22-*O*-beta-gluco-pyranosyl-mycotrienin-II | *B. megaterium* AHU 1375 | ansamycins | ND | Sugita *et al.*, 1985 |
| N-4909 | *Bacillus* sp. 4691 | cyclic acylpeptide | inhibition of tumor cell growth | Hiramoto *et al.*, 1996 |
| octapeptin D | *Bacillus* sp. JP-301 | peptide | against gram-positive and gram-negative bacteria | Shoji *et al.*, 1980 |
| octopyrin (thianosine) | *B. thiaminolyticus* | peptide | against bacteria | Katz and Demain, 1977 |
| oxetanocin | *B. megaterium* NK 84-0218 | ND | against viruses | Shimada *et al.*, 1986 |
| permetin A | *B. circulans* AJ 3902 | peptide | against gram-positive and gram-negative bacteria | Takahara *et al.*, 1979 |
| plipastatin | *B. cereus* BMG 302-F67 | ND | inhibition of phospholipase A2 | Umezawa *et al.*, 1986 |
| PM-94128 | *Bacillus* sp. PHM-PHD-090 | isocoumarin | inhibition of tumor cell growth | Canedo *et al.*, 1997 |
| polymixins A, B, D, E, F, M, P, S, T | *B. polymyxa* | polypeptides | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| polymyxin F | *B. circulans* ATCC 31228 | peptide | against bacteria | Parker *et al.*, 1977 |
| polymyxin P | *B. polymyxa* T-39 | peptide | against bacteria | Kimura *et al.*, 1969 |
| polymyxin TI | *B. polymyxa* E-12 | peptide | against bacteria | Shoji, Kato, and Hinoo, 1977 |

**Table 3.** Antibiotics elaborated by strains of *Bacillus* species (continued).

| Compounds | Strains | Structures | Activities | References |
|---|---|---|---|---|
| polypeptin | *B. circulans* | peptide | against bacteria | Katz and Demain, 1977 |
| proticin | *B. licheniformis* subsp. *mesentericus* ATCC 21552 | phosphorus-containing structure | against *E. coli*, *Proteus mirabilis*, and *Streptococcus haemolyticus* | Prave, Sukatsch, and Vertesy, 1972 |
| pumilacidins A-G | *B. pumilus* M 937-B1 | cyclic acyl-heptapeptides | against *Herpes simplex* virus type I | Naruse *et al.*, 1990 |
| pumilin | *B. pumilus* | peptide | against bacteria | Katz and Demain, 1977 |
| 2-methyl-4-[3]-quinazolinone | *B. cereus* BMH225-MF1 | ND | poly(ADP-ribose) synthase inhibitor | Yoshida *et al.*, 1991 |
| S-11-A | *B. circulans* S-11 mutant | 1-deamino-1-hydroxy xylostasin | against bacteria | Fujiwara *et al.*, 1980 |
| sattabacin, hydroxy-sattabacin, sattazolin, and methyl-sattazolin | *Bacillus* sp. B-60 | ND | against *Herpes simplex* viruses type I and II | Lampis *et al.*, 1995 |
| simplexin | *B. simplex* | ND | against *Rhizoctinia solani* | Glasby, 1993 |
| SP 127 | *B. brevis* ATCC 8185 | peptide | against *Pseudomonas aeruginosa* | Kikuchi and Nakao, 1977 |
| spergualin | *B. laterosporus* | ND | against tumor cells | Takeuchi *et al.*, 1981 |
| SQ 26,517 | *Bacillus* sp. 11480 | beta lactone | against bacteria | Parker, Rathnum, and Liu, 1982 |
| subsporins A-C | *B. subtilis* PCI 219 | peptides | against *Piricularia oryzae* and *Trichophyton mentagrophytes* | Glasby, 1993 Ebata, Miyazaki, and Takahashi, 1969 |
| subtilin | *B. subtilis* | ND | against *Lactobacillus casei*, *Micrococcus conglomeratus*, and *S. aureus* | Glasby, 1993 |

**Table 3.** Antibiotics elaborated by strains of *Bacillus* species (continued).

| Compounds | Strains | Structures | Activities | References |
|---|---|---|---|---|
| subtilysin | *B. subtilis* | ND | against *Clostridium edematiens*, *E. coli*, *Pasturella* species, *Salmonella gardneri*, and *V. comma* | Glasby, 1993 |
| tatumine | *B. brevis* Vm 4-572-403 | peptide | inhibition of tumor cell growth | Heaney and Kurylo, 1980 |
| tetain | *B. pumilus* | peptide | against bacteria | Katz and Demain, 1977 |
| thianosine | *B. thiaminolyticus* | ND | against gram-negative bacteria | Glasby, 1993 |
| thiocillin III | *B. badius* AR-91 | ND | against gram-positive bacteria | Shoji *et al.*, 1976 |
| thiocillins I-II | *B. megaterium* I-13 | ND | against gram-positive bacteria | Shoji *et al.*, 1976 |
| TL-119 | *Bacillus* sp. TL-119 | peptide | against gram-positive bacteria | Shoji *et al.*, 1975 |
| tridecapeptins A-C | *B. polymyxa* E-23 | acyl trideca-peptides | against gram-positive and gram-negative bacteria | Shoji *et al.*, 1978 |
| tyrocidin | *B. brevis* | polypeptide | against gram-positive and gram-negative bacteria | Glasby, 1993 |
| xanthobacidin | *B. subtilis* | ND | against *Xanthomonas* species | Glasby, 1993 |
| xylostatin | *B. circulans* | peptide | against bacteria | Katz and Demain, 1977 |
| YM-47522 | *Bacillus* sp. YL-03709B | ND | against fungi, *Rhodotorula acuta*, and *Pichia angusta* | Shibazaki *et al.*, 1996 |

ND, No data.

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## 2.1 Chemistry of peptides

Most of peptide antibiotics elaborated by species of the genus *Bacillus* are described in Table 3. In general, these antibiotics are produced by strains of *Bacillus subtilis* and *Bacillus brevis*. Polymyxin and the closely related colistin, bacitracin, the tyrothricin complex (linear gramicidin plus tyrocidine), and gramicidin S have been used, to some extent. for antibacterial therapy. Most of the peptide antibiotics produced by bacilli are active against gram-positive bacteria. However, compounds such as polymyxin, colistin, and circulin exhibit activity almost exclusively upon gram-negative bacteria, whereas bacillomycin and mycobacillin are effective agents against molds and yeasts.

Frequently. peptide antibiotics contain amino acids, which are unique and are not found in proteins (Bodanszky and perlman, 1964). D-amino acids, basic amino acids (ornithine, diaminobutyric acid), β-amino acids, dehydroamino acids (dehydroalanine), and sulfur-containing amino acids (lanthionine) are often present (Lewis and Snell, 1951). Most of peptides are cyclic structures, however, a few are linear structures. Besides the cyclic nature of a molecule, there may be unusual linkages or arrangements of the amino acids in the antibiotics. There are many reports on cyclic peptides having oxazole and/or thiazole ring(s) from tunicates and terrestrial microorganisms. Very few peptides containing conjugated oxazole or thiazole ring(s) have been isolated from natural origin (Kobayashi *et al.*, 1995). Some marine *Bacillus* spp. produce peptide antibiotics such as halobacillin, a cyclic acylpeptide antibiotic, isolated from marine *Bacillus* sp. (Trischman, Jensen, and Fenical, 1994). Although bacilli mainly synthesize peptides, one should not lose sight of the fact that antibiotics belonging to other chemical classes are also produced by these microorganisms.

### 2.2 Chemistry of macrocyclic lactone

A wide variety of natural compounds, exhibiting antibacterial, antihelminthic, antitumor, and immunosuppressive activities, contain a polyketide-derived skeleton (Donadio *et al.*, 1993). The polyene macrolide antibiotics are a large group of natural products with over 200 members (Rychnovsky, 1995). Several members of this class, such as amphotericin B, nystatin, and pimaricin, are important antifungal agents and have been used extensively in medicine. All of these natural products are macrolides that incorporate a conjugated polyene ranging from three to seven double bonds in length. They also contain a polyol section made up of a sequence of 1,2-, 1,3-, and 1,4-diols with 1,3-diols being the most common. Several members of this class have a sugar, usually the amino sugar β-mycosamine, attached by a β-linkage to one of the alcohols in the macrolide ring. The polyene macrolide antibiotics can be further divided into two groups: those that have the polyene across the ring from the lactone carbonyl and those that have the polyene in conjugation with the lactone. The oxo polyene macrolide antibiotics have been isolated from actinomyces soil bacteria, usually of the genera *Streptomyces*. The oxo polyene macrolides are listed in Table 4.

**Table 4.** Some oxo polyene macrolide antibiotics produced by *Streptomyces* species

| Species[a] | Antibiotics[a] |
|---|---|
| *S. viridogriseus* Thirum | dermostatin B |
| *S. ruber* | mycoticin B |
| *S. roseoflavus* ARIA 1951 subsp. *jenesis* JA 5068 | roflamycoin |
| *Actinomyces roseoflavus* subsp. *roseofungini* | roseofungin |
| *Streptomyces* sp. X-14994 | roxaticin |
| *A. surgutus* | surgumycin |

[a]Data from Rychnovsky, 1995.

Macrolide natural products (Table 4) generally possess even-numbered macrocyclic lactone rings (Kobayashi, Takahashi, and Ishibashi, 1995). However, several odd-numbered macrolides were recently isolated from the laboratory-cultured marine dinoflagellates *Amphidinium* sp., which are found in Okinawan marine flatworms, *Amphiscolops* sp. Some marine macrolides have other unique structural features such as having a variety of novel backbone-skeletons, which cannot be accounted for the normal polyketide biosynthesis produced by terrestrial microorganisms.

### 2.3 Chemistry of nucleosides

Nucleoside natural products are important chemical models for drug discovery and therapeutic intervention in human diseases including cancer, fungal infections, and viral infections related to human immunodeficiency viruses (HIVs). More than 200 known naturally occurring nucleoside antibiotics including several highly modified nucleosides isolated from marine invertebrates. Since the Bergmann's pioneering work on isolation of marine nucleosides from a Caribbean sponge in the 1950's, which led to the development of a recognized drug, Ara-C, several biologically active nucleosides have been reported from marine organisms, including sponges, gorgonians, nudibranchs, and seaweeds (Kato *et al.*, 1985).

### 2.4 Chemistry of diketopiperazines (DKPs)

2,5-Diketopiperazines, 2,5-dioxopiperazines, cyclic dipeptides and their derivatives are widely distributed in nature as secondary metabolites and some of them have unique bioactivities such as antimicrobial and antitumor activities (Kanzaki *et al.*, 1997). DKPs are ubiquitous throughout nature and are most commonly isolated from terrestrial yeast, lichen and fungi culture filtrates and are also observed in the culture

broths of marine bacteria and marine actinomycetes (Adamczeski, Reed, and Crews, 1995). Other examples of DKPs from marine sources include the isolation of *cyclo*-(glycyl-L-prolyl) from the starfish *Luidia clatharata* and of *cyclo*-(alanyl-prolyl) from marine bacteria associated with sponges. To date, DKPs have also been isolated from the following marine sponges: *Jaspis* sp., *Tedania ignis*, *Dysidea fragilis*, *Dysidea herbacea*, *Geodia baretti*, and *Leucophloeus fenestrata*. These unique compounds were very minor constituents of the extracts and this fact, together with the structural characteristics of the compounds, has provided a basis for hypothesis that such metabolites might actually be produced by microorganisms living on the invertebrates. Support for this idea is provided in report that *cyclo*-(prolyl-leucyl), *cyclo*-(prolyl-valyl), and *cyclo*-(prolyl-glycyl) are produced by a bacterium *Micrococcus* sp. associated with sponge *Tedania ignis*. The significance of isolating these DKPs from a marine bacterium associated with *T. ignis* resides in Schmitz's report of these same DKPs from extracts of the sponge. Given the propensity of microorganisms to produce low yield of DKPs and the consistent association of this *Micrococcus* with *T. ignis*, there is substantial cause to believe that these compounds are actually produced by the bacterium living in association with the sponge. However, it is now known that most culturable unicellular marine bacteria produce similar or identical DKPs (Unson and Faulkner, 1993). It seems reasonable to propose that the production of secondary metabolites by a symbiont would benefit a host if the chemicals deter potential predators and/or competitors.

The marine organisms live in unique association with a larger amount of symbionts such as bacteria than of their cell (Hirata and Uemura, 1986). As expected, the unusual metabolites of marine microorganisms may be concentrated in the whole body. Although many of the metabolites of marine microorganisms are similar to or identical

with those of terrestrial microorganisms, it would be necessary to multiply examples because of difficulties in the definition of a marine microorganism. In order to find the metabolites of marine microorganisms which differ from those of terrestrial microorganisms, it is necessary to study on minor bioactive constituents screened with the major compounds, on the basis of ecology of the marine organisms. For example, westiellamide isolated from terrestrial blue-green alga *Westiellopsis prolifera* (Prinsep *et al.*, 1992) appears to be identical to cycloxazoline isolated from marine ascidian *Lissoclinum bistratum* (Hambley *et al.*, 1992). The fact that the same cyclicpeptide occurs in a terrestrial cyanophyte and a marine symbiotic alga provides evidence that this compound isolated from marine ascidian originate from the symbiotic microorganisms. Marine natural products are generally assumed to be produced by the organism from which they are extracted. This assumption, which provides the basis for chemotaxonomy, is not always justified since marine invertebrates can accumulate bioactive metabolites from their microbial symbionts (Bewley, Holland, and Faulkner, 1996). However, despite considerable speculation, it is rare to find the major metabolites of an marine invertebrate located exclusively in associated microorganisms.

During the course of experiments conducted at the Marine Natural Products Research Unit, Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, Chulalongkorn University, diketopiperazines, macrolactins, cyclic tetrapeptide and 2'-deoxyadenosine have been isolated from marine bacteria collected from Sichang Island. An overall review on the structures, sources, and biological activity of these compounds (diketopiperazines, macrocyclic lactones, cyclic peptides, and purine nucleosides) is shown in Tables 5-8.

**Table 5.** Sources of diketopiperazines

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 1a | *cyclo*-(L-Pro-L-Leu) | bacterium *Streptomyces griseus* and fungus *Aspergillus fumigatus* | antimicrobial activity against *S. aureus* | Johnson, Jackson, and Eble, 1951 |
| 1a<br>2a | *cyclo*-(L-Pro-L-Leu)<br>*cyclo*-(L-Pro-L-Val) | algae *Scenedesmus* sp. | ND | Luedemann *et al.*, 1961 |
| 2a | *cyclo*-(L-Pro-L-Val) | bacterium *Streptomyces* sp. No. K-73 | ND | Ogura, Furuhata, and Furuhata 1975 |
| | | sponge *Leucophloeus fenestrata* | | Omar *et al*, 1988 |
| 1a<br>2a<br>3 | *cyclo*-(L-Pro-L-Leu)<br>*cyclo*-(L-Pro-L-Val)<br>*cyclo*-(Pro-Ala) | sponge *Tedania ignis* | ND | Schmitz *et al.*, 1983 |
| | | bacterium *Micrococcus* sp. | | Stierle, Cardellina, and Singleton, 1988 |
| 4 | *cyclo*-(Pro-Gly) | starfish *Lucidia clathrata* | ND | Pettit *et al.*, 1973 |
| 1<br>3<br>4<br>5<br>6<br>7<br>8<br>9<br>10 | *cyclo*-(Pro-Leu)<br>*cyclo*-(Pro-Ala)<br>*cyclo*-(Pro-Gly)<br>*cyclo*-(Pro-Phe)<br>*cyclo*-(Val-Phe)<br>*cyclo*-(Ala-Val)<br>*cyclo*-(Ala-Gly)<br>*cyclo*-(Ala-Phe)<br>*cyclo*-(Gly-Phe) | roasted cocoa bean | bitter taste | Pickenhagen *et al.*, 1975 |
| 1<br>2<br>3<br>5a<br>5b<br>11<br>12 | *cyclo*-(Pro-Leu)<br>*cyclo*-(Pro-Val)<br>*cyclo*-(Pro-Ala)<br>*cyclo*-(L-Pro-L-Phe)<br>*cyclo*-(L-Pro-D-Phe)<br>*cyclo*-(Pro-Hle)<br>*cyclo*-(L-Pro-L-Tyr) [maculosin] | fungus *Alternaria alternata* | [5a and 12] host-specific phytotoxic activity against spotted knapweed, *Centaurea maculosa* Lam. | Stierle, Cardellina, and Strobel, 1988 |
| 12<br>13 | *cyclo*-(L-Pro-L-Tyr) [maculosin]<br>*cyclo*-(*trans*-4-hydroxy-L-Pro-L-Phe) | sponge *Jaspis digonoxea* | ND | Rudi *et al.*, 1994 |

**Table 5.** Sources of diketopiperazines (continued)

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 13 | *cyclo*-(*trans*-4-hydroxy-L-Pro)-L-Phe) | unidentified *Jaspidae* sponge | ND | Adamczeski *et al.*, 1989 |
| 1a<br>2a<br>5a<br>12<br><br>14a<br>15a | *cyclo*-(L-Pro-L-Leu)<br>*cyclo*-(L-Pro-L-Val)<br>*cyclo*-(L-Pro-L-Phe)<br>*cyclo*-(L-Pro-L-Tyr) [maculosin]<br>*cyclo*-(L-Pro-L-Ile)<br>*cyclo*-(L-Pro-L-Met) | sponge-associated bacterium *Pseudomonas aeruginosa* | inactive against cytotoxic and antimicrobial activities | Jayatilake *et al.*, 1996 |
| 1b<br>1c<br>2b<br>5c<br>14a<br>16 | *cyclo*-(L-Pro-D-Leu)<br>*cyclo*-(D-Pro-D-Leu)<br>*cyclo*-(L-Pro-D-val)<br>*cyclo*-(D-Pro-D-Phe)<br>*cyclo*-(L-Pro-L-Ile)<br>*cyclo*-(4-methyl-D-Pro-L-Nva) | cyanobacterium (symbiosis with sponge *Calyx* cf. *podatypa*) | ND | Adamczeski *et al.*, 1995 |
| 17 | *cyclo*-(L-Pro-L-Trp) [brevianamide-F] | fungus *Penicillium brevi-compactum* Dierckx | ND | Birch and Russell, 1972 |
| | | bacterium *Vibrio* sp. (symbiosis with sponge *Hyrtios altum* | | Kobayashi *et al.*, 1994 |
| 18<br><br>19 | prolyl-2-(1',1'-dimethylallyl) tryptophyldiketopiperazine<br>12,13-dehydropropyl-2-(1',1'-dimethylallyl) tryptophyldiketopiperazine | terrestrial fungus *Penicillium italicum* | ND | Scott *et al.*, 1974; and Ogura, Furuhata, and Furuhata, 1975 |
| 20 | 1-*N*-methylalbonoursin | phytopathogenic fungus *Alternaria alternata* | ND | Liebermann *et al.*1988; and Gurney and Mantle, 1993 |
| | | bacterium *Streptomyces albus* | | Robins and Sefton, 1984 |

**Table 5.** Sources of diketopiperazines (continued)

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 21 | *cyclo*-(L-Pro-L-thioPro) | sponge *Tedania ignis* | inactive against brine shrimp cytotoxic, phytotoxic, plant growth regulatory, antimicrobial, and insecticidal activities | Dillman and Cardellina, 1991 |
| 22-23 | polychlorinated diketopiperazines | cyanobacterium *Oscillatoria spongeliae* (symbiosis with sponge *Dysidea herbacea*) | ND | Unson and Faulkner, 1993 |
| 24 | *cyclo*-(L-Arg-dehydrotyrosine) | sponge *Anthosigmella* aff. *raromicro-sclera* | metamorphosis inducer on ascidian larvae | Tsukamoto *et al.*, 1995 |
| 25<br>26<br>27<br>28 | 3-benzylidene-6-isobutylidene-2,5-dioxopiperazine<br>3,6-dibenzylidene-2,5-dioxopiperazine<br>3-benzyl-6-benzylidene-2,5-dioxopiperazine<br>3,6-dibenzyl-2,5-dioxopiperazine | bacterium *Streptomyces noursei* | ND | Brown, Kelley, and Wiberley, 1965 |
| 29 | neoechinulin | fungus *Aspergillus amstelodami* | ND | Barbettea *et al.*, 1969 |
| 30 | cryptoechinuline A | fungus *Aspergillus amstelodami* | ND | Cardillo *et al.*, 1974 |
| 31<br>32<br>33 | cycloechinulin<br>*N*-methylepiamauromine<br>epiamauromine | fungus *Aspergillus ochraceus* (NRRL 3519) | reduction in weight gain of corn earworm *Helicoverpa zea* | Guzman and Gloer, 1992 |
| 34 | austamide | fungus *Aspergillus ustus* | toxic metabolite to ducklings | Steyn, 1971 |
| 35 | lanosulin | fungus *Penicillium lanosum* | ND | Dix, Martin, and Moppett, 1972 |

**Table 5.** Sources of diketopiperazines (continued)

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 36 | 2-benzyl-1,4-dimethyl-5-hydroxymethyl-2,5-*epi*-dithia-3, 6-diketopiperazine | unidentified fungus | antifungal and antibacterial activities | DeVault and Rosenbrook, 1973 |
| 37 | 2-benzyl-1,4-dimethyl-5-hydroxymethyl-2,5-*epi*-trithia-3, 6-diketopiperazine | | | |
| 38 | bisdethiadi (methylthio) analogue of 2-benzyl-1,4-dimethyl-5-hydroxymethyl-2,5-*epi*-dithia-3,6-diketopiperazine | | | |
| 39 | tryptophan-dehydrobutyrine diketopiperazine | bacterium *Streptomyces spectabilis* | reverse transcriptase inhibitor | Kakinuma and Rinehart, 1974 |
| 40 | diketopiperazine derived from trichloroleucine | sponge *Dysidea herbacea* | ND | Kazlauskas *et al.*, 1978 |
| 41 | verruculogen | fungus *Penicillium verruculosum* | causing severe tremorgenic reaction in mice | Uramoto *et al.*, 1982 |
| 42 | acetoxyl derivative of verruculogen | | | |
| 43 | gliotoxin E | fungus *Penicillium terlikowskii* | Immunomodula-ting activity | Waring *et al.*, 1987 |
| 44 | gliotoxin | fungus *Dichotomomy-ces cejpii* | antifungal activity against *C. albicans* and *C. tropicalis* | Kaouadji *et al.*, 1990 |
| 45 | gliovictin | marine fungus *Asteromyces cruciatus* | ND | Shin and Fenical, 1987 |
| 46 | verrucofortine | fungus *Penicillium verrucosum* var. *cyclopium* | inactive neurotoxic activity | Hodge, Harris, and Harris, 1988 |
| 47 | etzionin | unidentified Red sea tunicate | antifungal activity against *C. albicans* | Hirsch *et al.*, 1989 |
| 48 | aurantiamine | terrestrial fungus *Penicillium aurantiogrise-um* | ND | Larsen, Frisvad, and Jensen, 1992 |
| 49 | dysamide A | sponge *Dysidea fragilis* | ND | Su *et al.*, 1993 |
| 50 | dysamide B | | | |
| 51 | dysamide C | | | |
| 52 | dysamide D | | | Fu *et al.*, 1997 |

**Table 5.** Sources of diketopiperazines (continued)

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 53 | fructigenine A | fungus *Penicillium aurantiogrise-um* | ND | Boyes-Korkis *et al.*, 1993 |
| 54<br>55 | Sch 54794<br>Sch 54796 | terrestrial fungus *Tolypocladium* sp. | [55] platelet aggregating factor (PAF) inhibitors | Chu *et al.*, 1993 |
| 56<br>57 | WIN 64821<br>WIN 64745 | soil fungus *Aspergillus* sp. | substance P (SP) antagonists | Barrow *et al.*, 1993 |
| 58<br>59<br>60<br>61<br>62<br>63 | leptosin A<br>leptosin B<br>leptosin C<br>leptosin D<br>leptosin E<br>leptosin F | marine fungus *Leptosphaeria* sp. (symbiosis with algae *Sargassum tortile*) | cytotoxic activity against P388 tumor cells | Takahashi *et al.*, 1994 |
| 64 | diketopiperazine of *N*-methyltyrosine | soil bacterium *Streptomyces griseus* (SC 488) | calpain inhibitor | Alvarez *et al.*, 1994 |
| 65<br>66<br>67<br>68<br>69 | TAN-1496 A<br>TAN-1496 B<br>TAN-1496 C<br>TAN-1496 D<br>TAN-1496 E | soil fungus *Microsphaerop-sis* sp. FL-16144 | mammalian DNA topoisomerase I inhibitors | Funabashi *et al.*, 1994 |
| 70 | 1'-(2-phenyl-ethylene)-ditryptophenaline | fungus *Aspergillus flavus* SC1661 | substance P antagonist | Barrow and Sedlock, 1994 |
| 71<br>72 | Sch 52900<br>Sch 52901 | fungus *Gliocladium* sp. SCF-1168 | inhibitors of *c-fos* protoonco-gene induction | Chu *et al.*, 1995 |
| 73 | macrophominol | fungus *Macrophomina phaseolina* | phytotoxic activity | Trigos, Reyna, and Matamo-ros, 1995 |
| 41<br>74<br>75<br>76<br>77<br><br>78<br>79 | verruculogen<br>fumitremorgin B<br>fumitremorgin C<br>demethoxyfumitremorgin C<br>12,13-dihydroxyfumitremor-gin C<br>tryprostatin A<br>tryprostatin B | fungus *Aspergillus fumigatus* BM 939 | M phase inhibitors of the mammalian cell cycle | Cui, Kakeya, and Osda, 1996 |
| 80<br>81 | spirotryprostatin A<br>spirotryprostatin B | fungus *Aspergillus fumigatus* | cell cycle inhibitors | Cui, Kakeya, and Osda, 1996 |

**Table 5.** Sources of diketopiperazines (continued)

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 82<br>83<br>84<br>85 | cyclotryprostatin A<br>cyclotryprostatin B<br>cyclotryprostatin C<br>cyclotryprostatin D | fungus *Aspergillus fumigatus* BM939 | cell cycle inhibitors | Cui, Kakeya, and Osda, 1997 |
| 86 | pallidin | sponge *Rhaphisia pallida* | ND | Su *et al.*, 1996 |
| 87<br>88 | XR330<br>XR334 | soil bacterium *Streptomyces* sp. | inhibitors of plasminogen activators | Bryans *et al.*, 1996 |
| 89 | dipodazine | fungus *Penicillium dipodomyis* | ND | Sorensen *et al.*, 1999 |

ND, No data.

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**Table 6.** Sources of macrocyclic lactones

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 90<br>91 | flavofungin A<br>flavofungin B | bacterium *Streptomyces flavofungini* | antifungal activity | Bognar *et al.*, 1970 |
| 92 | swinholide A | Red sea sponge *Theonella swinholei* | antifungal and cytotoxic activities against L1210 and KB tumor cells | Carmely and Kashman, 1985; and Doi M *et al*, 1991 |
| 92<br>93<br>94<br>95 | swinholide A<br>swinholide B<br>swinholide C<br>isoswinholide A | Okinawan sponge *Theonella swinhoei* | cytotoxic activity against KB tumor cells | Kobayashi *et al.*, 1970; and Kobayashi *et al.*, 1989 |
| 96<br>97<br>98<br>99 | swinholide D<br>swinholide E<br>swinholide F<br>swinholide G | Okinawan sponge *Theonella* sp. | cytotoxic activity against L1210 and KB tumor cells | Tsukamoto *et al.*, 1991 |
| 100 | tedanolide | Caribbean sponge *Tedania ignis* | cytotoxic activity against KB tumor cells | Schmitz *et al.*, 1984 |
| 101<br>102 | acutiphycin<br>20,21-didehydroacutiphycin | freshwater blue-green algae *Oscillatoria acutissima* | cytotoxic activity against KB and murine Lewis lung tumor cells | Barchi, Moore, and Patterson, 1984 |
| 103 | kabiramide C | unidentified nudibranch eggmasses | antifungal activity | Matsunaga, Fusetani, and Hashimoto, 1986 |
| 104<br>105<br>106<br>107<br>108<br>109 | kabiramide A<br>kabiramide B<br>kabiramide D<br>kabiramide E<br>dihydrohalichondramide<br>33-methyldihydrohalichon-dramide | eggmasses of nudibranch *Hexabranchus* sp. | cytotoxic activity against L1210 tumor cells and inhibition of cell division of fertilized sea urchin eggs | Matsunaga *et al.*, 1989 |
| 110<br>108<br>111<br>112 | halichondramide<br>dihydrohalichondramide<br>isohalichondramide<br>imide of halichondramide | Pacific sponge *Halichondria* sp. | antifungal actvity against *C. albicans* and *T. mentagro-phyte* | Kernan and Faulkner, 1987; and Kerman *et al.*, 1988 |
| 103<br>108<br>113 | kabiramide C<br>dihydrohalichondramide<br>tetrahydrohalichondramide | Spanish nudibranch *Hexabranchus sanguineus* | | Kernan, Molinski, and Faulkner, 1988 |

**Table 6.** Sources of macrocyclic lactones (continued)

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 114<br>115 | ulapualide A<br>ulapualide B | eggmasses of nudibranch *Hexabranchus sanguineus* | cytotoxic activity against L1210 tumor cells and anti-fungal activity against *C. albicans* | Roesener and Scheuer, 1986 |
| 116<br>117<br>118<br>119<br>120 | amphidinolide A<br>amphidinolide B<br>amphidinolide C<br>amphidinolide D<br>amphidinolide E | marine dinoflagellate *Amphidinium* sp. (symbiosis with Okinawan flatworm *Amphiscolops* sp.) | cytotoxic activity against L1210 and L5178Y tumor cells | Kobayashi, Ishibashi, and Hirota, 1986; Ishibashi *et al.*, 1987; Kobayashi *et al.*, 1988; Kobayashi *et al.*, 1989; Kobayashi *et al.*, 1990; and Kobayashi, *et al.*, 1991 |
| 121<br>122<br>123 | amphidinolide F<br>amphidinolide G<br>amphidinolide H | marine dinoflagellate *Amphidinium* sp. (symbiosis with Okinawan flatworm *Amphiscolops magniviridis* | cytotoxic activity against L1210 and KB tumor cells | Kobayashi *et al.*, 1991; and Kikuchi *et al.*, 1991 |
| 124<br>125<br>126<br>127<br>128<br>129 | bistheonellide A<br>bistheonellide B<br>bistheonellide C<br>isobistheonellide A<br>bistheonellic acid A<br>bistheonellic acid B | sponge *Theonella* spp. | cytotoxic activity against L1210 and KB tumor cells and inhibit embryos of starfish *Asterina pectinifera* | Kato *et al.*, 1987; and Kobayashi *et al.*, 1991 |
| 130<br>131 | bistratene A<br>bistratene B | tunicate *Lissoclinum bistratum* | cytotoxic activity | Degnan *et al.*, 1989 |
| 132 | prorocentrolide | marine dinoflagellate *Prorocentrum lima* | toxin | Torigoe *et al.*, 1988 |

**Table 6.** Sources of macrocyclic lactones (continued)

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 133<br>134<br>135<br>136 | iejimalide A<br>iejimalide B<br>iejimalide C<br>iejimalide D | Okinawan tunicate *Eudistoma* cf. *rigida* | cytotoxic activity against L1210 and L5178Y tumor cells | Kobayashi *et al.*, 1988; and Kikuchi *et al.*, 1991 |
| 137 | goniodomin A | rock pool dinoflagellate *Goniodoma pseudogoniaulax* | antifungal activity against *C. albicans* and inhibition of cell division of fertilized sea urchin eggs | Murakami *et al.*, 1988 |
| 138<br>139<br>140<br>141<br>142<br>143 | macrolactin A<br>macrolactin B<br>macrolactin C<br>macrolactin D<br>macrolactin E<br>macrolactin F | unidentified gram-positive marine bacterium | antibacterial activity against *S. aureus* and *B. subtilis*; antiviral activity against *Herpes simplex viruses*; and cytotoxic activity against B16-F10 tumor cells | Gustafson, Roman, and Fenical, 1989; and Rychnovsky, *et al.*, 1992 |
| 144<br>145<br>146<br>147<br>148 | scytophycin A<br>scytophycin B<br>scytophycin C<br>scytophycin D<br>scytophycin E | terrestrial blue-green algae *Scytonema pseudohofmanni* | cytotoxic activity against KB and P388 tumor cells and antifungal activity against pathogenic fungi | Ishibashi *et al.*, 1986; and Carmeli *et al.*, 1990 |
| 145<br>149<br>150<br><br>151 | scytophycin B<br>6-hydroxyscytophycin B<br>6-hydroxy-7-*O*-methyl-scytophycin E<br>totytoxin | terrestrial blue-green algae *Scytonema mirabile* (Dillwyn) Bornet (strain BY-8-1) | cytotoxic activity against KB and LoVo tumor cells and antifungal activity against pathogenic fungi | Carmeli, Moore, and Patterson, 1990 |
| 145<br>149<br>152<br><br>148<br>150<br><br>151 | scytophycin B<br>6-hydroxyscytophycin B<br>19-*O*-demethyl-scytophycin B<br>scytophycin E<br>6-hydroxy-7-*O*-methyl-scytophycin E<br>tolytoxin | terrestrial blue-green algae *Scytonema burmanicum* Skuja (strain DO-4-1) | | |

**Table 6.** Sources of macrocyclic lactones (continued)

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 150<br>151<br>152 | 6-hydroxy-7-*O*-methyl-scytophycin E<br>tolytoxin<br>19-*O*-demethylscytophycin B | terrestrial blue-green algae *Scytonema ocellatum* Lyngbye ex Bornet & Flahault (strain FF-66-3) | cytotoxic activity against KB and LoVo tumor cells and antifungal activity against pathogenic fungi | Carmeli, Moore, and Patterson, 1990 |
| 151 | tolytoxin | terrestrial blue-green algae *Scytonema ocellatum* Lyngbye ex Bornet & Flahault (strain FF-65-1 and DD-8-1) | | |
| 153 | aplyronine A | sea hare *Aplysia kurodai* | cytotoxic activity | Ojika *et al.*, 1993 |
| 154<br>155<br>156<br>157 | sphinxolide A<br>sphinxolide B<br>sphinxolide C<br>sphinxolide D | Caledonian sponge *Neosiphonia superstes* | cytotoxic activity against NSCLC-N6, P388, KB, and HT29 tumor cells | D'Auria *et al.*, 1993 |
| 158<br>159 | reidispongiolide A<br>reidispongiolide B | Caledonian sponge *Reidispogia coerulea* | cytotoxic activity against various human tumor cells | D'Auria *et al.*, 1994 |
| 160 | zooxanthellatoxin A | symbiotic marine dinoflagellate *Symbiodinium* sp. (strain Y-6) | vasoconstrictors | Nakamura, Asari, and Murai, 1995 |
| 160<br>161 | zooxanthellatoxin A<br>zooxanthellatoxin B | | | Nakamura *et al.*, 1995 |
| 162 | callipeltoside A | Lithistida sponge *Callipelta* sp. | cytotoxic activity against NSCLC-N6 and P388 tumor cells | Zampella *et al.*, 1996 |
| 163<br>164 | callipeltoside B<br>callipeltoside C | Lithistida sponge *Callipelta* sp. | cytotoxic activity against P388 and KB tumor cells and antiviral activity against HIV | Zampella *et al.*, 1997 |

**Table 6.** Sources of macrocyclic lactones (continued)

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 165 | ossamycin | bacterium *Streptomyces hygroscopicus* var. *ossamyceticus* | cytotoxic activity | Kirst *et al.*, 1996 |
| 166<br>167<br>168<br>169 | halishigamide A<br>halishigamide B<br>halishigamide C<br>halishigamide D | Okinawan sponge *Halichondria* sp. | cytotoxic activity against L1210 and KB tumor cells and antifungal activity against *T. mentagrophytes* | Kobayashi *et al.*, 1997 |
| 170<br>171 | dolabellide C<br>dolabellide D | Japanese sea hare *Dolabella auricularia* | cytotoxic activity | Suenaga, *et al.*, 1997 |
| 172 | lyngbyaloside | marine cyanobacterium *Lyngbya bouillonii* | ND | Klien *et al.*, 1997 |
| 173<br>174<br>175<br>176 | amphilactam A<br>amphilactam B<br>amphilactam C<br>amphilactam D | sponges *Amphimedon* spp. | nematocidal activity against nematode *Haemonchus contortus* | Ovenden *et al.*, 1999 |
| 177 | streptovaricin C | soil bacterium *Streptomyces* sp. KMI-30 | antimutagenic activity against various mutagens | Ooka *et al.*, 1999 |
| 178 | methamycin B | bacterium *Actinomycete* sp. Y-8620959 | phytotoxic activity | Mukhopadhyay *et al.*, 1999 |
| 179 | tetrin C | soil bacterium *Streptomyces* sp. GK9244 | antifungal activity against *Mortierella ramanniaus* | Ryu *et al.*, 1999 |

ND, No data.

**Table 7.** Sources of cyclic peptides

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 180 | tentoxin | phytopathogenic fungus *Alternaria tenuis* Auct. | causing severe chlorosis in the cotyledons | Meyer *et al.*, 1971; Steele *et al.*, 1976; Pinet *et al.*, 1996; and Pinet *et al.*, 1996 |
| 181 | dihydrotentoxin | phytopathogenic fungus *Alternaria alternata* | phytotoxic activity | Liebermann *et al.*, 1988 |
| 182 | Cyl-2 | phytopathogenic fungus *Cyclindrocladi-um scoparium* | ND | Hirota *et al.*, 1973 |
| 183<br>184 | ulicyclamide<br>ulithiacyclamide | tuniate *Lissoclinum patella* | ND | Ireland and Scheuer, 1980 |
| 184<br>185 | ulithiacyclamide<br>ascidiacyclamide | unidentified ascidian | [185] cytotoxic activity against L1210 tumor cells | Hamamoto *et al.*, 1983; Ireland and Scheuer, 1980; and Hamada, Kato, and Shioiri, 1985 |
| 186 | bacillomycin D | bacterium *Bacillus subtilis* | antifungal activity | Peypoux *et al.*, 1981 |
| 187<br>188<br>189 | patellamide A<br>patellamide B<br>patellamide C | tunicate *Lissoclinum patella* | cytotoxic activity against L1210 tumor cells | Ireland *et al.*, 1982 |
| 190<br>191<br>192 | patellamide D<br>lissoclinamide 4<br>lissoclinamide 5 | | cytotoxic activity against MRC5CV1 and T24 tumor cells | Degnan, *et al.*, 1989; and Schmitz, *et al.*, 1989 |
| 193<br>194 | lissoclinamide 7<br>lissoclinamide 8 | | | Hawkins *et al.*, 1990 |
| 195 | HC-toxin | terrestrial fungus *Helminthosporium carbonum* | phytotoxic activity | Liesch *et al.*, 1982 |

**Table 7.** Sources of cyclic peptides (continued)

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 196<br>197<br>198 | discodermin B<br>discodermin C<br>discodermin D | sponge *Discodermia kiiensis* | antimicrobial activity against *P. aeruginosa*, *E. coli*, *B. subtilis* and *M. smegmatis*, and inhibit embryo development of starfish *Asterina pectinifera* | Matsunaga, Fusetani, and Konosu, 1985 |
| 199 | scytonemin A | soil blue-green algae *Scytonema* sp. | calcium antagonist | Helms *et al.*, 1988 |
| 200<br>201 | cyanogenosin-LA<br>cyanogenosin-RR | cyano-bacterium *Microcystis aeruginosa* | hepatotoxic activity | Painuly *et al.*, 1988 |
| 202<br>203 | fenestin A<br>fenestin B | Sponge *Leucophloeus fenestrata* | inactive cytotoxic activity against P388 and HT29 tumor cells | Omar *et al.*, 1988 |
| 204<br>205 | puwainaphycin C<br>puwainaphycin D | terrestrial blue-green algae *Anabaena* sp. | [204] positive cardiotonic activity in isolated mouse atria | Moore *et al.*, 1989 |
| 206<br>207 | bistratamide A<br>bistratamide B | tunicate *Lissoclinum bistratum* | cytotoxic activity | Degnan *et al.*, 1989 |
| 208<br>209 | bistratamide C<br>bistratamide D | | depressant activity | Foster *et al.*, 1992 |
| 210<br>211 | cyclotheonamide A<br>cyclotheonamide B | sponge *Theonella* sp. | thrombin inhibitors | Fusetani *et al.*, 1990. |
| 212 | orbiculamide A | | cytotoxic activity against P388 tumor cells | Fusetani, Sugawara, and Matsunaga, 1991 |
| 213 | keramamide A | sponge *Theonella* sp. | sarcoplasmic reticulum $Ca^{2+}$-ATPase inhibitor | Kobayashi *et al.*, 1991 |
| 214<br>215<br>216 | keramamide B<br>keramamide C<br>keramamide D | | inhibit superoxide generation response of human neutrophils | Kobayashi *et al.*, 1991 |

**Table 7.** Sources of cyclic peptides (continued)

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 217<br>218<br>219<br>220 | keramamide E<br>keramamide G<br>keramamide H<br>keramamide J | sponge *Theonella* sp. | cytotoxic activity against L1210 and KB tumor cells | Kobayashi *et al.*, 1995 |
| 221<br>222 | tawicyclamide A<br>tawicyclamide B | tunicate *Lissoclinum patella* | cytotoxic activity against human colon tumor cells | MaDonald *et al.*, 1992 |
| 223 | westiellamide or cycloxazoline | terrestrial blue-green algae *Westiellopsis prolifica* | cytotoxic activity against KB and LoVo tumor cells | Prinsep *et al.*, 1992 |
| | | tunicate *Lissoclinum bistratum* | cytotoxic activity against MRC5CV1 and T24 tumor cells | Hambley *et al.*, 1992 |
| 224 | hormothamnion A | cyano-bacterium *Hormotham-nion entero-morpholides* | cytotoxic and antimicrobial activities | Gerwick *et al.*, 1992 |
| 225 | mollamide | ascidian *Didemnum molle* | cytotoxic activity against P388, HT29 and CV1 tumor cells and inhibit RNA synthesis | Carroll *et al.*, 1994 |
| 226 | schizotrin A | terrestrial cyano-bacterium *Schizotrix* sp. | antibacterial activity against *S. aureus*, *S. albus*, *E. coli*, and *B. subtilis*, and antifungal activity against *S. cerevisiae*, *C. ablicans*, *C. tro-picalis*, *R. ruba*, *S. rolfsii*, *R. solani*, *F. oxy-sporum* and *C. gloeosporioides* | Pergament and Carmeli, 1994 |
| 227 | dolastatin E | sea hare *Dolabella auricularia* | cytotoxic activity | Ojika *et al.*, 1995 |

**Table 7.** Sources of cyclic peptides (continued)

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 228 | oscillamide Y | terrestrial cyano-bacterium *Oscillatoria agardhii* | chymotrypsin inhibitor | Sano and Kaya, 1995 |
| 229 | cyclodidemnamide | ascidian *Didemnum molle* | cytotoxic activity against human colon tumor cells | Boden, Norley, and Pattenden, 1996 |
| 230 | P951 | cyano-bacterium *Aphanocapsa feldmanni* (symbiosis with sponge *Theonella swinhoei*) | antifungal activity | Bewley *et al.*, 1996 |
| 231<br>232 | raocyclamide A<br>raocyclamide B | marine cyano-bacterium *Oscillatoria raoi* | [231] inhibit cell division of sea urchin embryos (*Paracentrotus lividus*) | Admi, Afek, and Carmeli, 1996; and Freeman and Pattenden, 1998 |
| 233 | apicidin | fungus *Fusarium* spp. (ATCC 74289 and ATCC 74322) | antiprotozoal activity against *Apicomplexan* parasites and antimalarial activity against *Plasmodium berghei* | Darkin-Rattray *et al.*, 1996 |
| 234<br>235<br>236 | anabaenopeptin B<br>anabaenopeptin E<br>anabaenopeptin F | cyano-bacterium *Oscillatoria agardhii* (NIES-204) | rat aortic relaxant | Shin *et al.*, 1997 |
| 237<br>238<br>239<br>240 | loloatin A<br>loloatin B<br>loloatin C<br>loloatin D | tropical marine bacterium | antimicrobial activity against methicillin resistant *S. aureus*, vancomycin-resistant enterococci, and drug-resistant *S. pneumoniae* | Gerard *et al.*, 1999 |

ND, No data.

**Table 8.** Sources of purine nucleosides and derivatives

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 241 | 1-methylisoguanosine | sponge *Tedania digitata* | reduced muscle relaxation and hypothermia in mice; hypotensive, bradycardia, antiinflammatory and anti-allergic activities in rats | Quinn *et al.*, 1980 |
| 242<br>243 | mycalisine A<br>mycalisine B | sponge *Mycale* sp. | inhibit cell division of fertilized starfish eggs | Kato *et al.*, 1985 |
| 244 | doridosine (N-methylpurine riboside) | nudibranch *Anisodoris nobilis* | hypotensive and bradycardia activities | Fuhrman *et al.*, 1980 |
| 245 | isoguanosine (oxyadenosine or crotonoside) | nudibranch mollusc *Diaulula sandiegensis* | hypotensive and bradycardia activities; relaxation of smooth muscle; and stimulate accumulation of cyclic adenosine-3',5' monophosphate phosphodiesterase in brain tissue | Fuhrman *et al.*, 1981 |
| 246 | aplysidine | Okinawan sponge *Aplysina* sp. | adenosine $A_1$ receptor antagonist | Kondo *et al.*, 1992 |
| 247 | 7-deazainosine | ascidian *Aplidium pantherinum* | inactive cytotoxic activity against P388 tumor cell | Kim *et al.*, 1993 |
| 248 | tubercidin | marine bacterium *Streptomyces* sp. | antiviral activity | Kazlauskas *et al.*, 1983 |
| 249 | 5-iodo-5'-deoxytubercidin | red algae *Hypnea valendiae* | muscle relaxant and blocker of polysynaptic and monosynaptic reflexes | Kazlauskas *et al.*, 1983 |
| 250<br>251 | 5'-deoxy-3-bromotubercidin<br>5'-deoxytubercidin | ascidian *Didemnum voeltzkowi* | ND | Mitchell *et al.*, 1996 |

**Table 8.** Sources of purine nucleosides and derivatives (continued)

| No. | Compounds | Sources | Activities | References |
|---|---|---|---|---|
| 252 | angustmycin A (decoyinine) | marine bacterium *Streptomyces hygroscopicus* var. *decoyicus* | antibacterial activity against *Streptococcus feacalis* and cytotoxic activity | McCarthy *et al.*, 1968 |
| 253 | aristeromycin | marine bacterium *Streptomyces citricolor* | inhibitory activity against *Pyricularia oryzae* and *Xanthomonas oryzae* | Kishi *et al.*, 1972 |
| 254 | adenosine | sponge *Tethya aurantia* | cardiodepressor | Weber *et al.*, 1981 |
| 255<br>256 | 9-$\beta$-D-arabinofuranosyl-adenine (ara A)<br>3'-*O*-acetyl-9-$\beta$-D-arabino-furanosyladenine | gorgonian *Eunicella cavolini* | antiviral activity | Cimino, Rosa, and Stefano, 1984 |
| 257 | 9-[5'-deoxy-5'-(methylthio)-$\beta$-D-xylofuranosyl]adenine | nudibranch mollusc *Doris verrucosa* | ND | Cimino *et al.*, 1986 |
| 258 | 5'-deoxy-5'-dimethyl-arsinyladenosine | kidney of giant clam *Tridacna maxima* | ND | Francesconi *et al.*, 1991 |
| 259<br>260 | 2'-deoxyguanosine<br>2'-deoxyinosine | acorn worm *Ptychodera flava* | ND | Sakemi, and Higa, 1985; and Dematte *et al.*, 1985 |
| 261<br>262 | trachycladine A<br>trachycladine B | sponge *Trachycladus laevispirulifer* | [261] cytotoxic activity against leukemia, colon, and breast tumor cells; [262] ND | Searle and Molinski, 1995 |

ND, No data.

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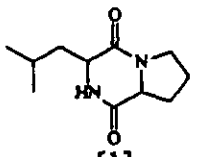

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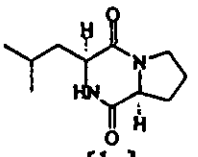
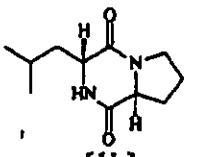


[1a]
*cyclo*-(L-Pro-L-Leu)



[1b]
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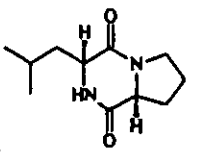

[1c]
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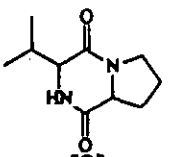

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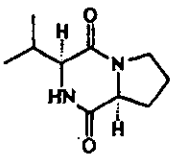
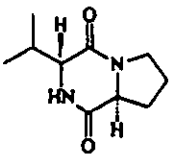
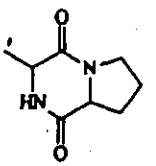


[2a]
*cyclo*-(L-Pro-L-Val)



[2b]
*cyclo*-(L-Pro-D-Val)



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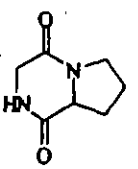
*cyclo*-(Pro-Ala)



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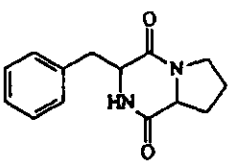
*cyclo*-(Pro-Gly)



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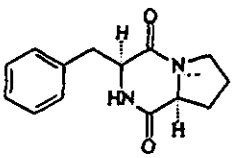
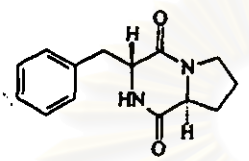
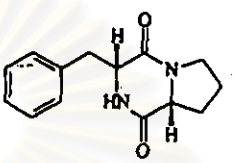


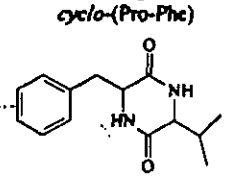
[5a]
*cyclo*-(L-Pro-L-Phe)



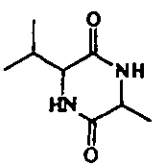
[5b]
*cyclo*-(L-Pro-D-Phe)



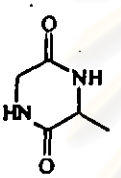
[5c]
*cyclo*-(D-Pro-D-Phe)



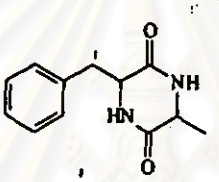
[6]
*cyclo*-(Phe-Val)



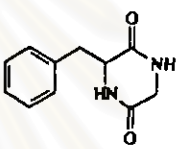
[7]
*cyclo*-(Ala-Val)



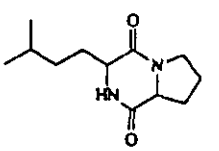
[8]
*cyclo*-(Ala-Gly)



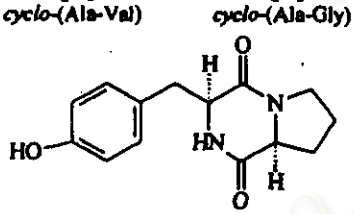
[9]
*cyclo*-(Ala-Phe)



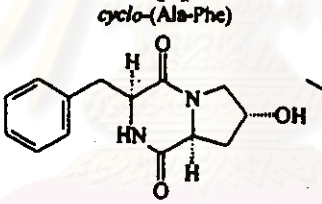
[10]
*cyclo*-(Gly-Phe)



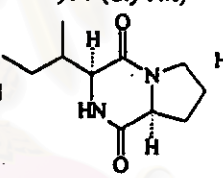
[11]
*cyclo*-(Pro-Hle)



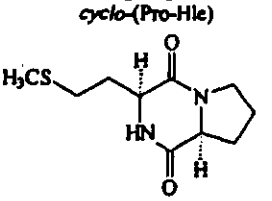
[12]
*cyclo*-(L-Pro-L-Tyr) [maculosin]



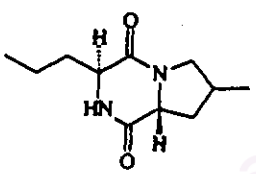
[13]
*cyclo*-(L-*trans*-(4-hydroxy-Pro)-L-Phe)



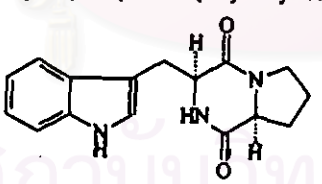
[14a]
*cyclo*-(L-Pro-L-Ile)



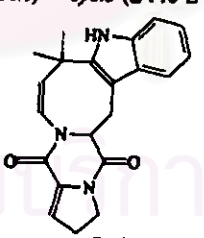
[15b]
*cyclo*-(L-Pro-L-Met)



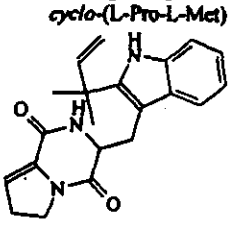
[16]
*cyclo*-(4-methyl-D-Pro-L-Nval)



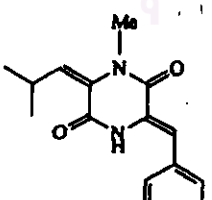
[17]
*cyclo*-(L-Pro-L-Trp) [brevianamide-F]



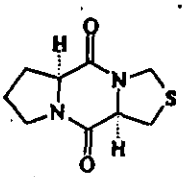
[18]
prolyl-2(1',1'-dimethylallyl)
tryptophanyldiketopiperazine



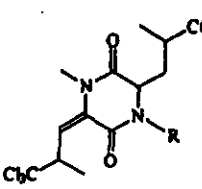
[19]
12,13-dehydroprolyl-2-
(1',1'-dimethylallyl)
tryptophanyldiketopiperazine



[20]
1-*N*-methylalbonoursin

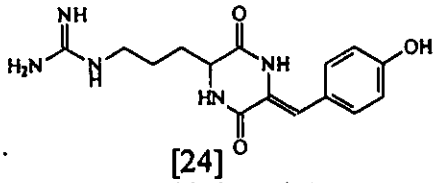


[21]
*cyclo*-(L-Pro-L-thioPro)

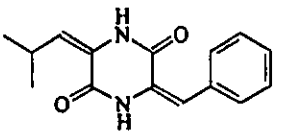


[22] polychlorinated
diketopiperazine
R = $CH_3$

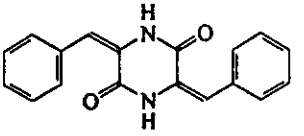
[23] polychlorinated
diketopiperazine
R = H



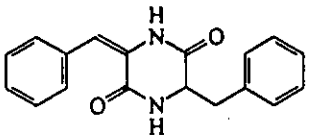
[24]
*cyclo*-(l-Arg-dehydrotyrosine)



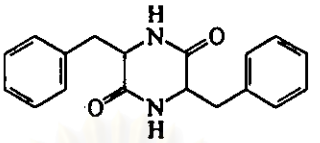
[25]
3-benzylidene-6-isobutylidene-
2,5-dioxopiperazine



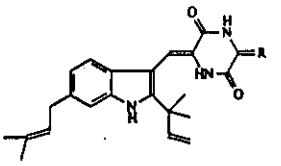
[26]
3,6-dibenzylidene
2,5-dioxopiperazine



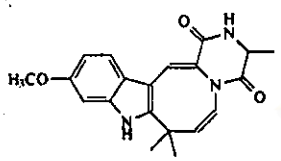
[27]
3-benzyl-6-benzylidene-
2,5-dioxopiperazine



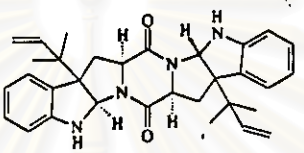
[28]
3,6-dibenzyl-
2,5-dioxopiperazine



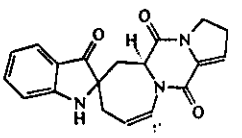
[29] neoechinuline, R = O
[30] crytoechinuline A, R = $CH_2$



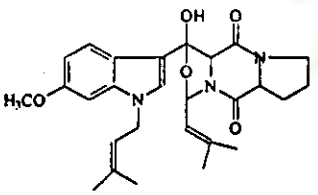
[31]
cycloechinuline



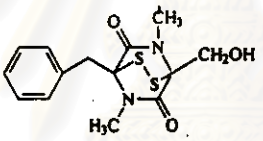
[32] N-methylepiamauromine, R = CH3
[33] epiamauromine, R = H



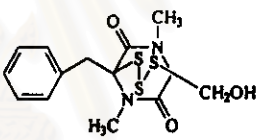
[34]
austamine



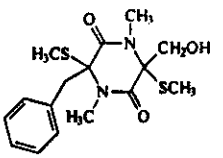
[35]
lanosulin



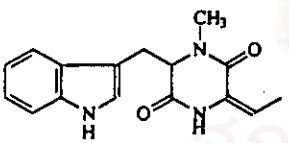
[36]
2-benzyl-1,4-dimethyl-
5-hydroxymethyl-2,5-*epi*-
dithia-3,6-diketopiperazine



[37]
2-benzyl-1,4-dimethyl
5-hydroxymethyl-2,5-*epi*-
trithia-3,6-diketopiperazine

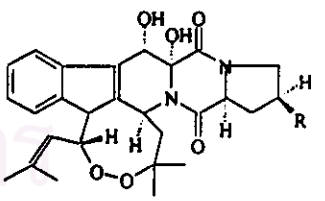


[38]
bisdethiadi(methylthio)
analog of 2-benzyl-1,4-dimethyl-
5-hydroxymethyl-2,5-*epi*-dithia-
3,6-diketopiperazine

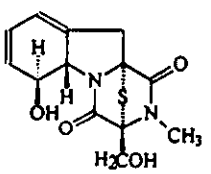


[39]
trypthophan-dehydrobutyrine

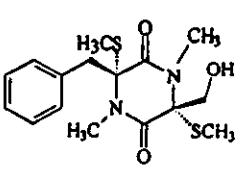
[40]
diketopiperazine derived
from trichloroleucine



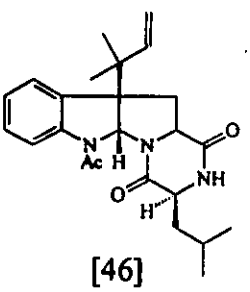
[41] verruculogen, R = H
[42] acetoxyl derivative of
verruculogen, R = $OCOCH_3$



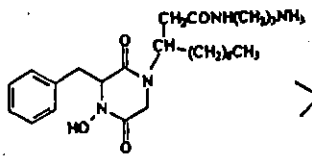
[43] gliotoxin E, n = 3
[44] gliotoxin, n = 2



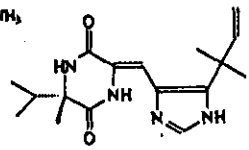
[45]
gliovictin



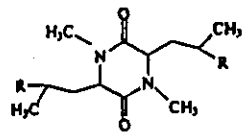
[46]
verrucofortine



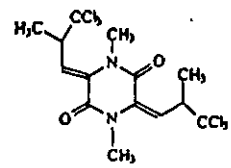
[47]
etzionin



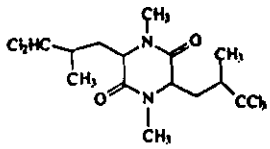
[48]
aurantiamine



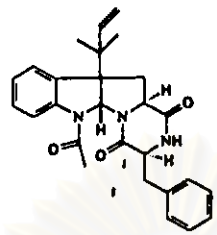
[49] dysamide A, R = $CCl_3$
[50] dysamide B, R = $CHCl_2$



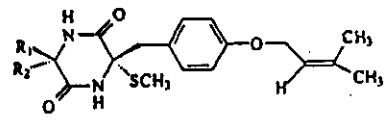
[51]
dysamide C



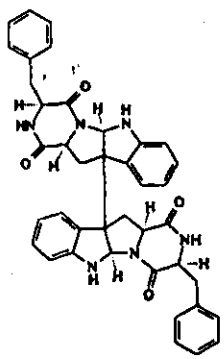
[52]
dysamide D



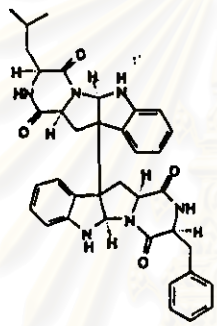
[53]
fructigenine



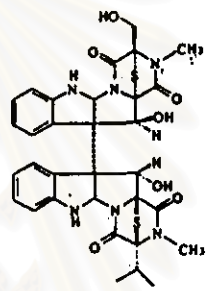
[54] Sch 54794, $R_1$ = H, $R_2$ = $SCH_3$
[55] Sch 54796, $R_1$ = $SCH_3$, $R_2$ = H



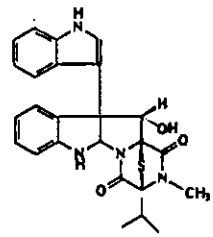
[56]
WIN 64821



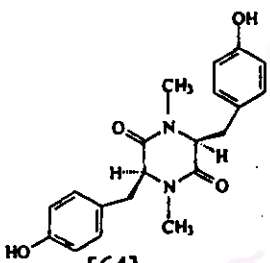
[57]
WIN 64745



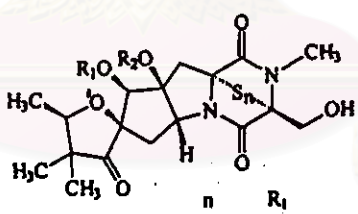
[58] leptosin A, R = 4
[59] leptosin B, R = 3
[60] leptosin C, R = 2



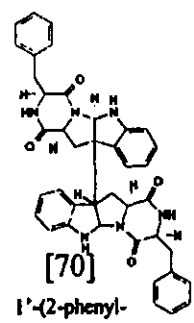
[61] leptosin D, R = 2
[62] leptosin E, R = 3
[63] leptosin F, R = 4



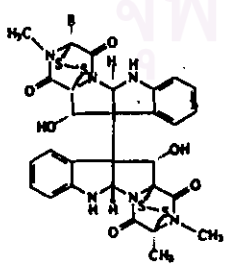
[64]
diketopiperazine of
*N*-methyltyrosine



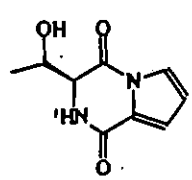
| | | n | $R_1$ | $R_2$ |
|---|---|---|---|---|
| [65] | TAN-1496 A | 2 | $OCOCH_3$ | $OCOCH_3$ |
| [66] | TAN-1496 B | 2 | $OCOCH_3$ | H |
| [67] | TAN-1496 C | 3 | $OCOCH_3$ | $OCOCH_3$ |
| [68] | TAN-1496 D | 2 | H | H |
| [69] | TAN-1496 E | 4 | $OCOCH_3$ | $OCOCH_3$ |



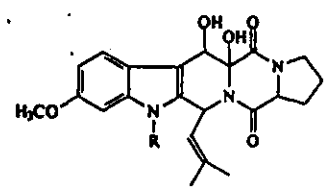
[70]
1'-(2-phenyl-
ethylene)-
ditryptophenaline



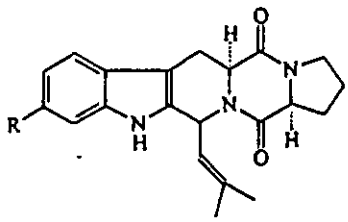
[71] Sch 52900, R = $CH(OH)CH_3$
[72] Sch 52901, R = $CH_2CH_3$



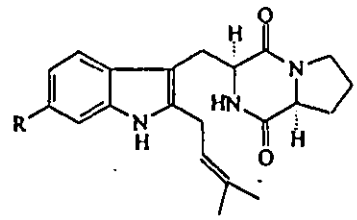
[73]
macrophominol



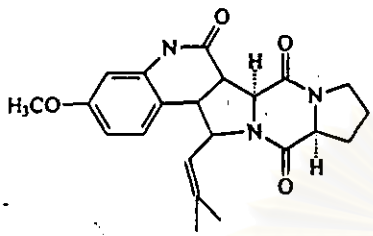
[74] fumitremorgin B, R = isopropyl
[77] 12,13-dihydroxyfumitremorgin C, R = H



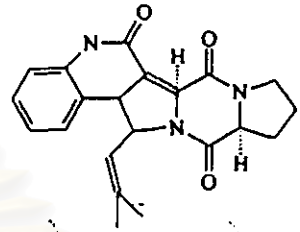
[75] fumitremorgin C, R = $CH_3O$
[76] demethoxyfumitremorgin C, R = H



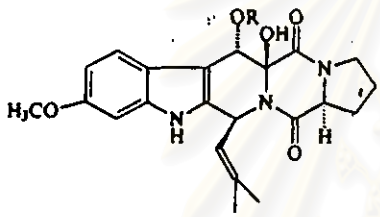
[78] tryptostatin A, R = $CH_3O$
[79] tryptostatin B, R = H



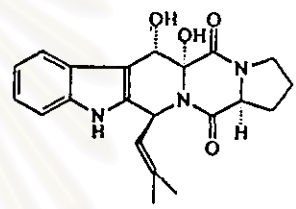
[80]
spirotryprostatin A



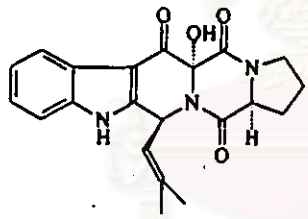
[81]
spirotryprostatin B



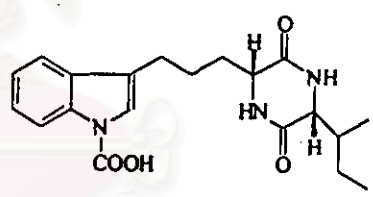
[82] cyclotryprostatin A, R = H
[83] cyclotryprostatin B, R = $CH_3$



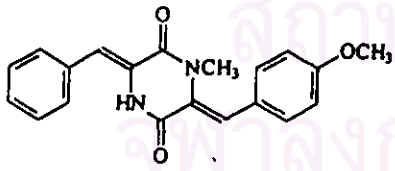
[84]
cyclotryprostatin C



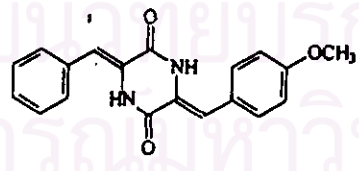
[85]
cyclotryprostatin D



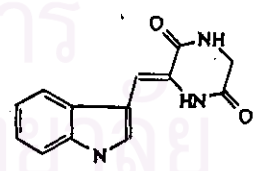
[86]
pallidin



[87]
XR 330



[88]
XR 334



[89]
dipodazine

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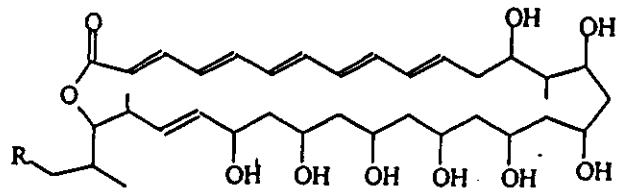
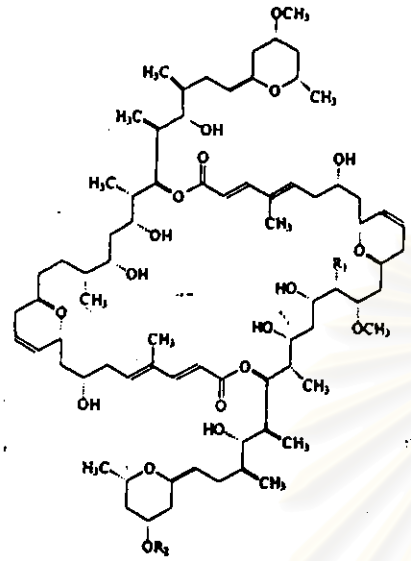
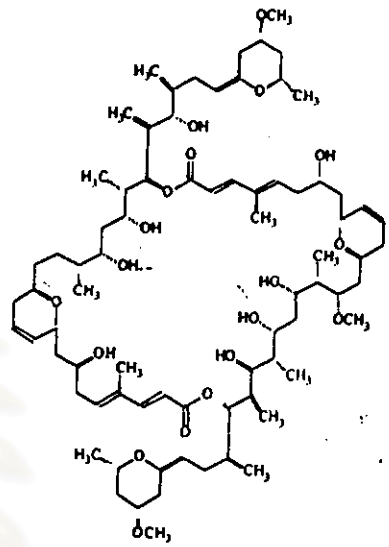


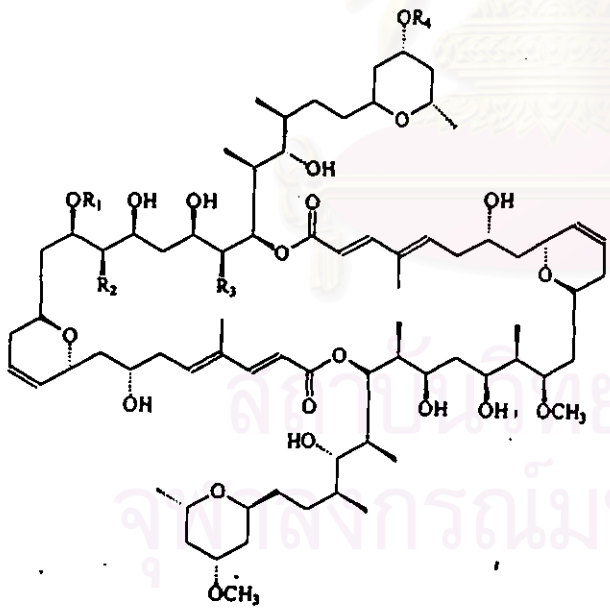
[90] flavofungin A, R = H
[91] flavofungin B, R = $CH_3$



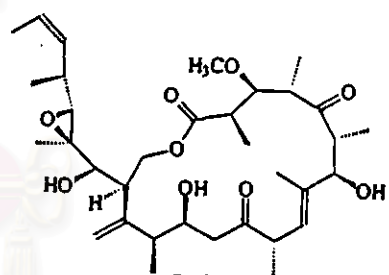
[92] swinholide A, $R_1 = CH_3$, $R_2 = CH_3$
[93] swinholide B, $R_1 = H$, $R_2 = CH_3$
[94] swinholide C, $R_1 = CH_3$, $R_2 = H$



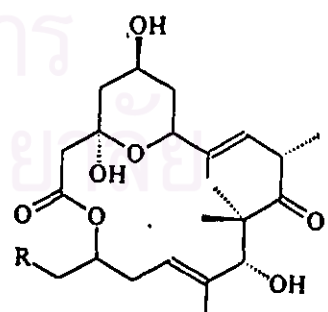
[95]
isoswinholide A



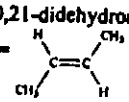
[96] swinholide D, $R_1 = H$, $R_2 = R_3 = R_4 = CH_3$
[97] swinholide E, same as [96] except that the substituent at C-6' is OH
[98] swinholide F, same as [96] except that the confoguration at C-2' is Z
[99] swinholide G, $R_1 = R_2 = R_4 = CH_3$, $R_3 = H$

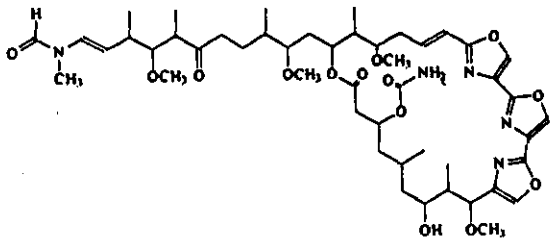


[100]
tedanolide

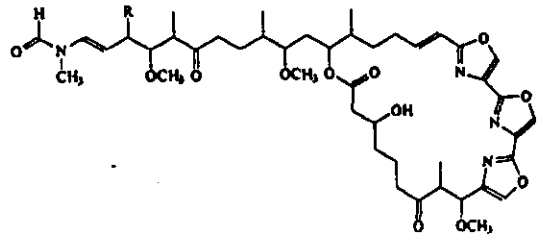


[101] acutiphycin
R = $CH_3CH_2CH_2CH_2$
[102] 20,21-didehydroacutiphycin
R =

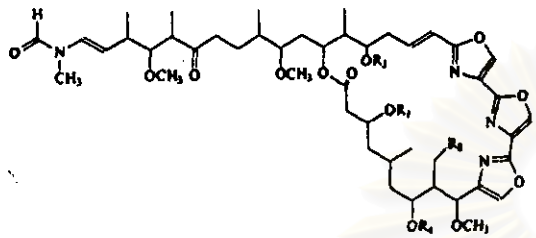




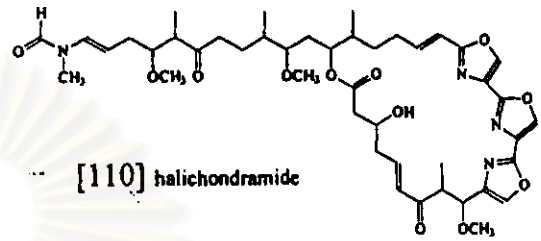
[103]
kabiramide C



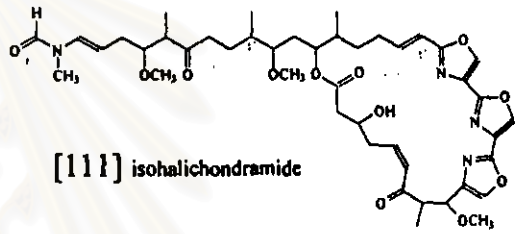
[108] dihydrohalichondramide, R = H
[109] 33-methyldihydrohalichondramide, R = $CH_3$



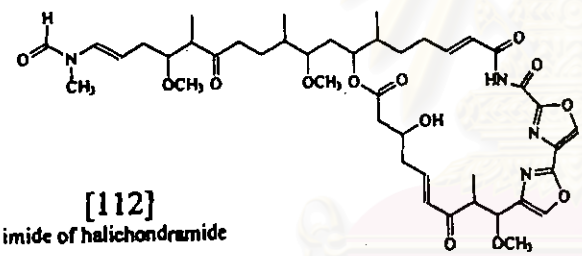
[104] kabiramide A, $R_1$ = $CONH_2$, $R_2$ = OH, $R_3$ = $CH_3$, $R_4$ = H
[105] kabiramide B, $R_1$ = $CONH_2$, $R_2$ = $R_3$ = $R_4$ = H
[106] kabiramide D, $R_1$ = $R_2$ = $R_4$ = H, $R_3$ = $CH_3$
[107] kabiramide E, $R_1$ = $COCH_3$, $R_2$ = H, $R_3$ = $CH_3$, $R_4$ = H



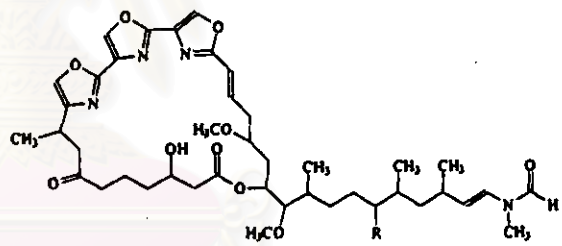
[110] halichondramide



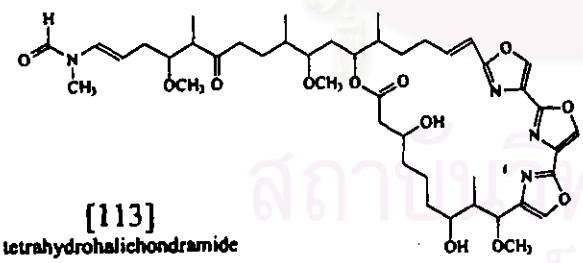
[111] isohalichondramide



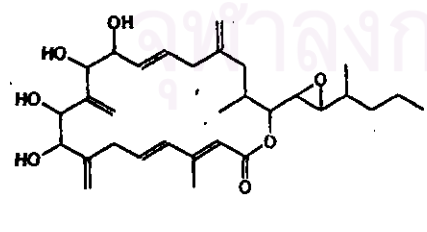
[112]
imide of halichondramide



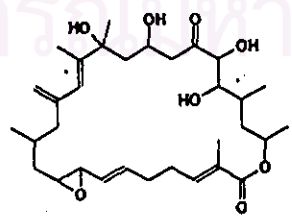
[114] ulapualide A, R = O
[115] ulapulide B, R =



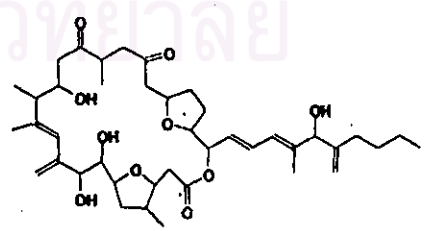
[113]
tetrahydrohalichondramide



[116]
amphidinolide A



[117] amphidinolide B
[118] amphidinolide D



[119]
amphidinolide C

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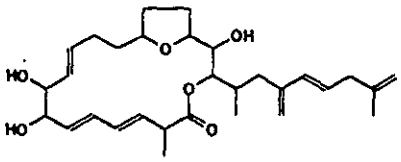
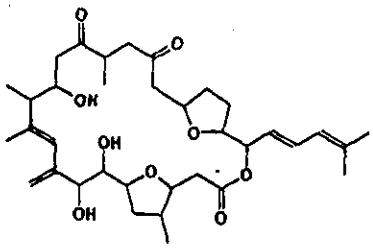
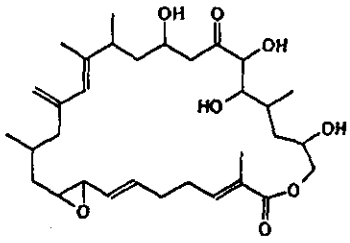


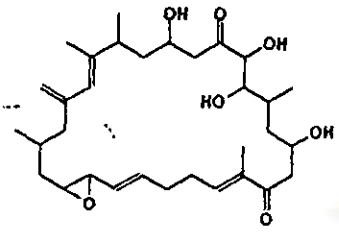
[120]
amphidinolide E



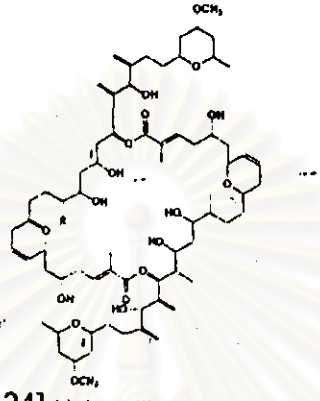
[121]
amphidinolide F



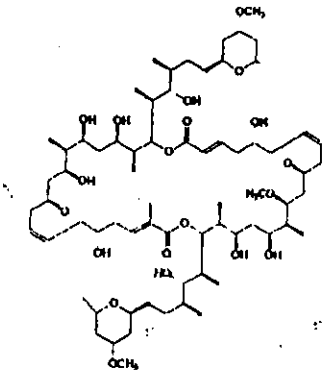
[122]
amphidinolide G



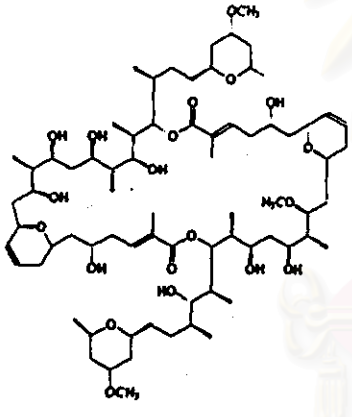
[123]
amphidinolide H



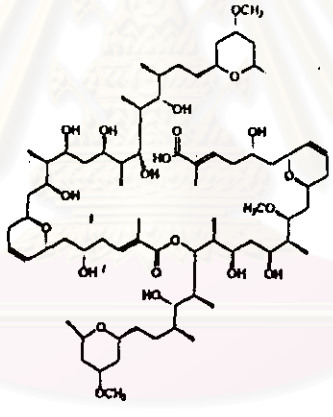
[124] bistheonellide A, R = H
[125] bistheonellide B, R = $CH_3$



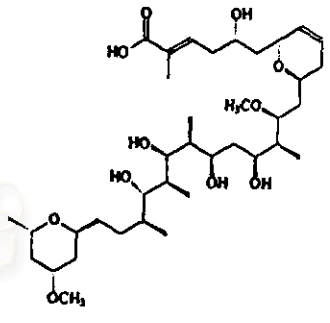
[126]
bistheonellide C



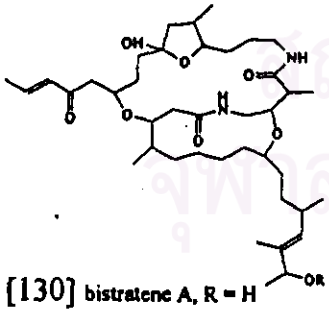
[127] isobistheonellide A



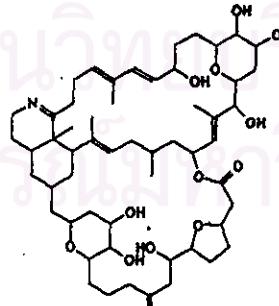
[128] bistheonellic acid A



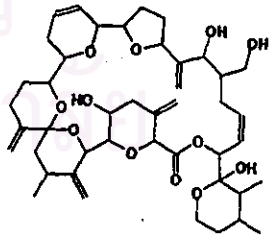
[129] bistheonellic acid B



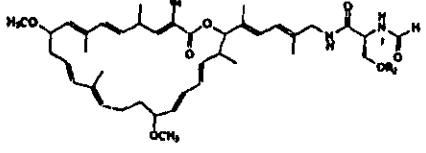
[130] bistratene A, R = H
[131] bistratene B, R = $COCH_3$



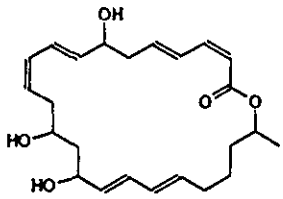
[132] prorocentrolide



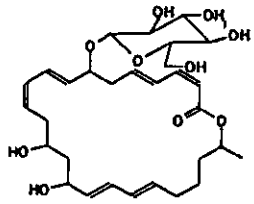
[137] goniodominA



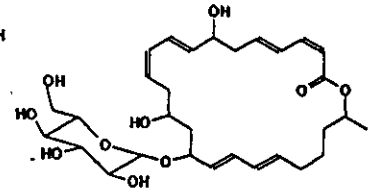
[134] iejimalide B, $R_1 = CH_3$, $R_2 = H$
[135] iejimalide C, $R_1 = H$, $R_2 = SO_3Na$
[136] iejimalide D, $R_1 = CH_3$, $R_2 = SO_3Na$



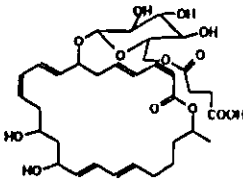
[138] macrolactin A



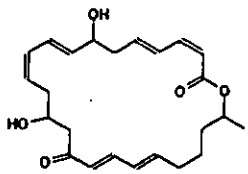
[139] macrolactin B



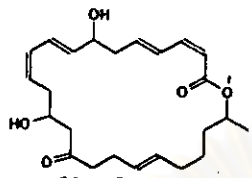
[140] macrolactin C



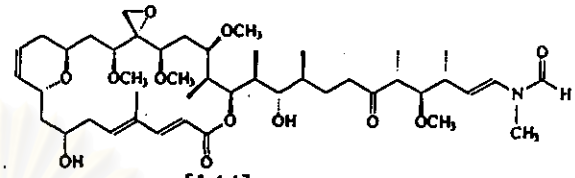
[141] macrolactin D



[142] macrolactin E



[143] macrolactin F



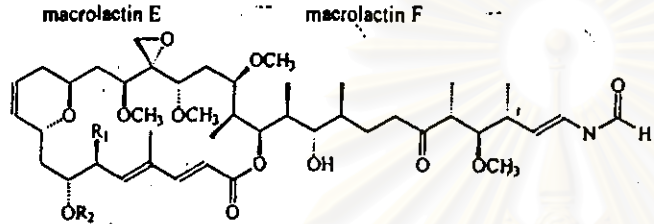
[144] scytophycin A

[145] scytophycin B, at C-27

[146] scytophycin C, at C-16

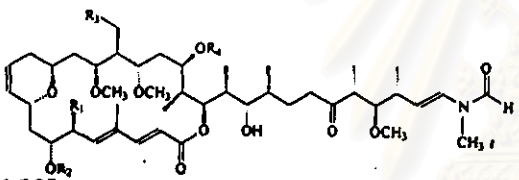
[147] scytophycin D, at C-16

[148] scytophycin E, at DC-16



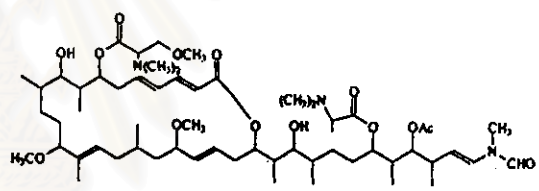
[149] 6-hydroxyscytophycin B, $R_1$ = OH, $R_2$ = H

[151] tolytoxin, $R_1$ = OH, $R_2$ = $CH_3$

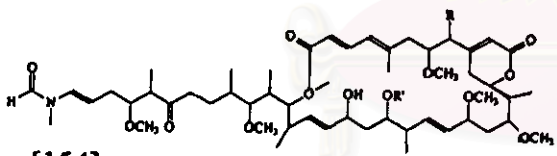


[150] 6-hydroxy-7-*O*-methylscytophycin E, $R_1$ = $R_2$ = $R_3$ = $R_4$ = H

[151] 19-*O*-demethylscytophycin B, $R_1$ = $R_3$ = OH, $R_2$ = $R_4$ = $CH_3$



[153] aplyronine

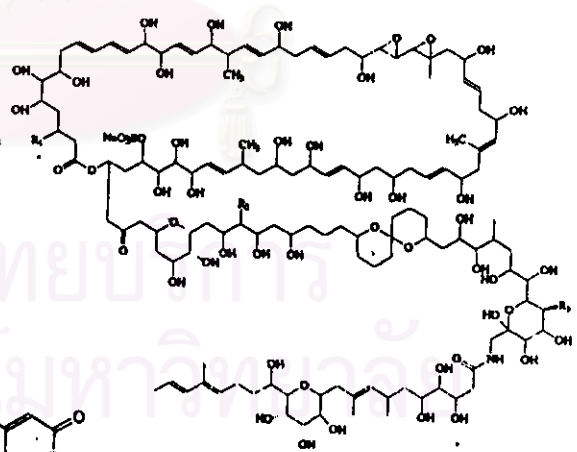


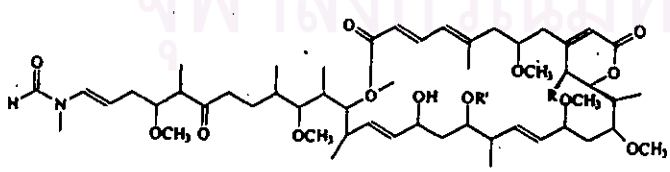
[154] sphinxolide A, R = $OCH_3$, R' = H

[155] sphinxolide B, R = R' = H

[156] sphinxolide C, R = $OCH_3$, R' = $CH_3$

[157] sphinxolide D, R = H, R' = $CH_3$

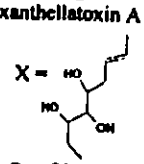




[158] reidispongiolide A, R = H, R' = $CH_3$

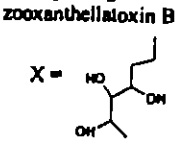
[159] reidispongiolide B, R = H, R' = H

[160] zooxanthellatoxin A

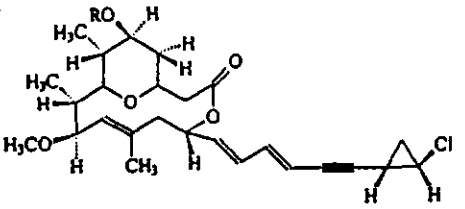


$R_1$ = H, $R_2$ = OH, $R_3$ = OH

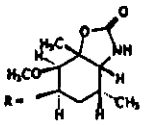
[161] zooxanthellatoxin B



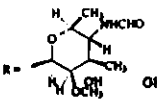
$R_1$ = OH, $R_2$ = H, $R_3$ = H



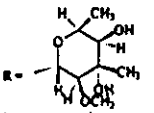
[162] callipeltoside A

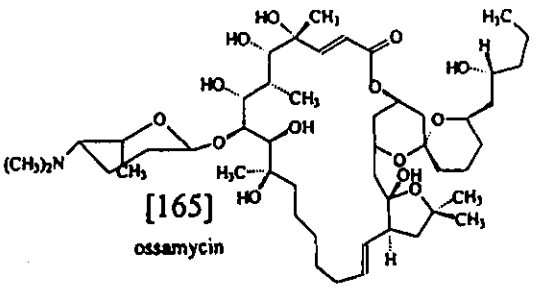


[163] callipeltoside B

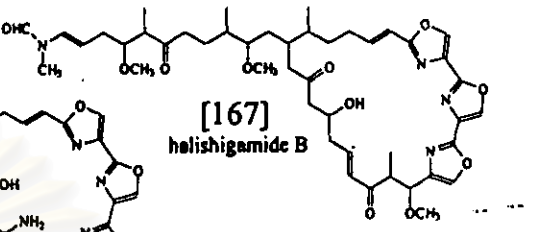


[164] callipeltoside C

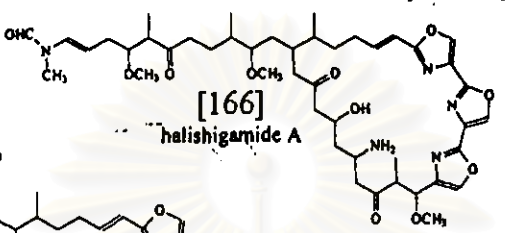




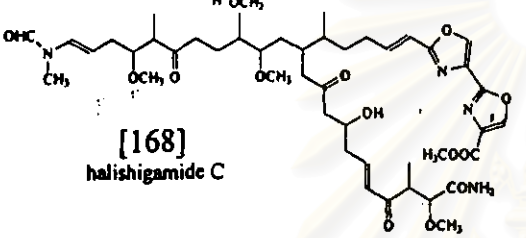
[165] ossamycin



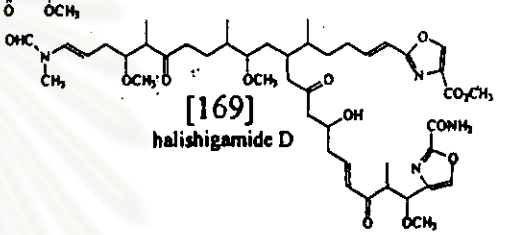
[167] halishigamide B



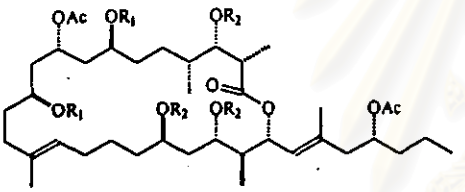
[166] halishigamide A



[168] halishigamide C

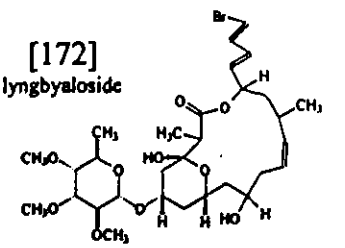


[169] halishigamide D

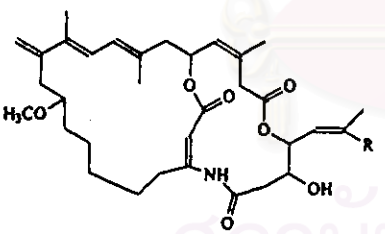


[170] dolabelide C, $R_1$ = $OCOCH_3$, $R_2$ = H

[171] dolabelide D, $R_1$ = $R_2$ = H

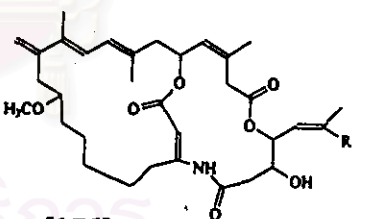


[172] lyngbyaloside



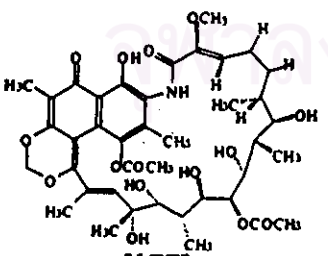
[173] amphilactam A, R = H

[174] amphilactam B, R = $CH_3$

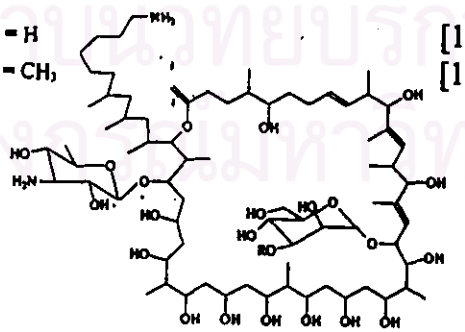


[175] amphilactam C, R = H

[176] amphilactam D, R = $CH_3$

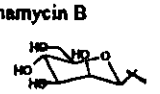


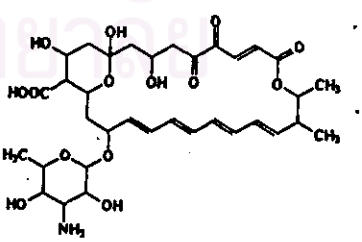
[177] streptovaricin C



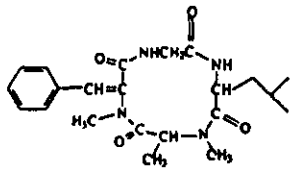
[178] methamycin B

R =

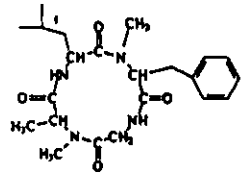




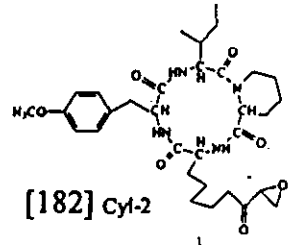
[179] tetrin C



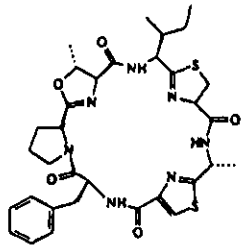
[180] tentoxin



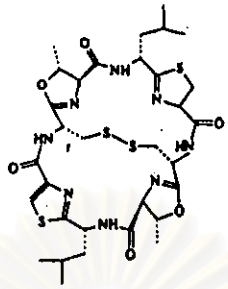
[181] dihydrotentoxin



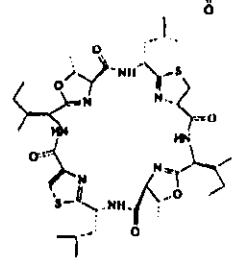
[182] Cyl-2



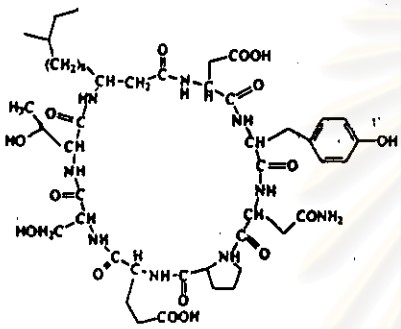
[183] ulicyclamide



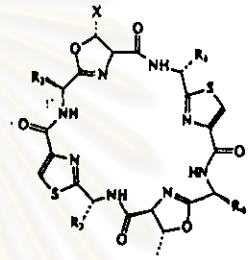
[184] ulithiacyclamide



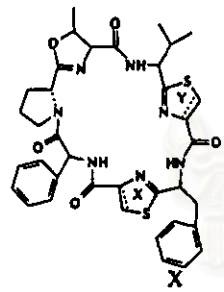
[185] ascidiacyclamide



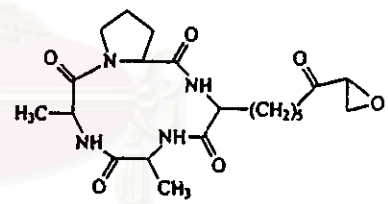
[186] bacillomycin D



| Name | X | $R_1$ | $R_2$ | $R_3$ | $R_4$ |
|---|---|---|---|---|---|
| patellamide A | H | D-Val | L-Ile | D-Val | L-Ile |
| patellamide B | $CH_3$ | D-Ala | L-Leu | D-Phe | L-Ile |
| patellamide C | $CH_3$ | D-Ala | L-Val | D-Phe | L-Ile |
| patellamide D | $CH_3$ | D-Ala | L-Ile | D-Phe | L-Ile |



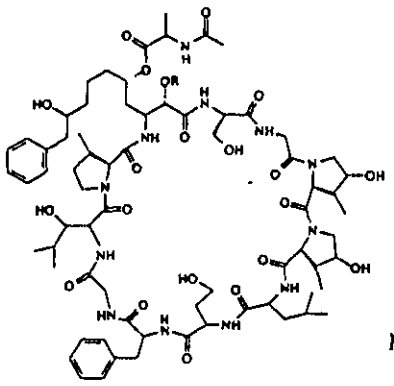
| | X | Y |
|---|---|---|
| [191] lissoclinamide 4 | thiazole | thiazoline |
| [192] lissoclinamide 5 | thiazole | thiazole |
| [193] lissoclinamide 7 | thiazoline | thiazoline |
| [194] lissoclinamide 8 | thiazole | thiazoline |



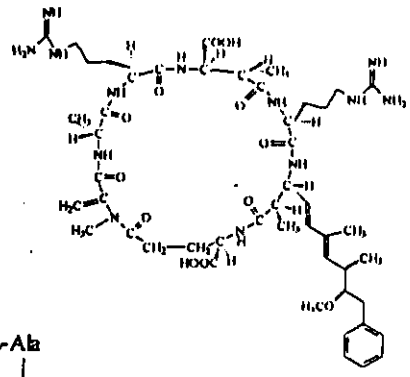
[195] HC-toxin

HCO-D-Ala-L-Phe-L-Pro-X-D-Trp-L-Arg-D-Cys(O 3H)-L-Thr-L-MeGln-D-Leu-LAsn-L-Thr-Sar

[196] discodermin B, X = D-Val-L-*t*-Leu
[197] discodermin C, X = D-*t*-Leu-L-Val
[198] discodermin D, X = D-Val-L-Val



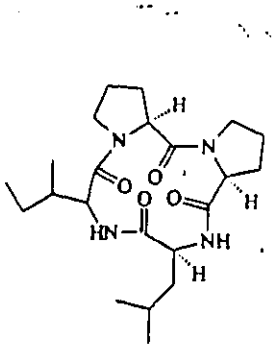
[199] scytophycin A



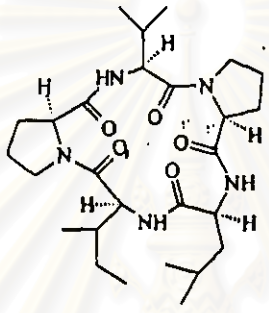
MeDhAla-D-Ala-L-Leu-D-MeAsp-L-Ala
D-Glu(iso)-Beta-Amino acid

[200] cyanogenosin-LA

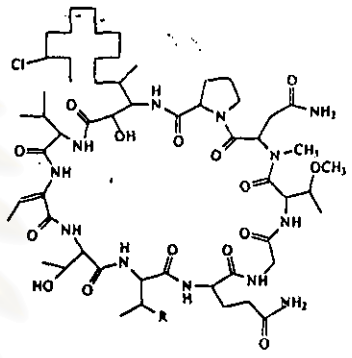
[201] cyanogenosin-RR



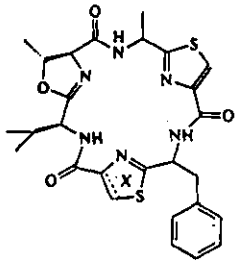
[202] fenestin A



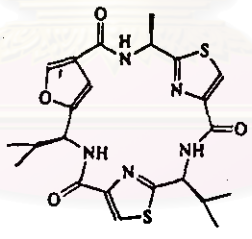
[203] fenestin



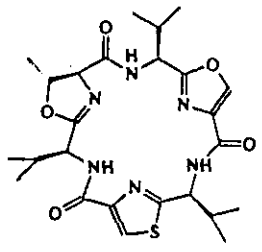
[204] puwainaphycin C, R = OH
[205] puwainaphycin D, R = $CH_3$



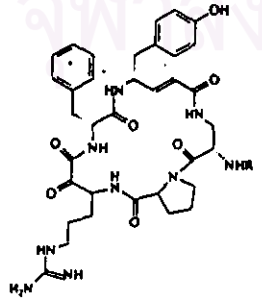
[206] bistratamide A, X = thiazoline
[207] bistratamide B, X = thiazole



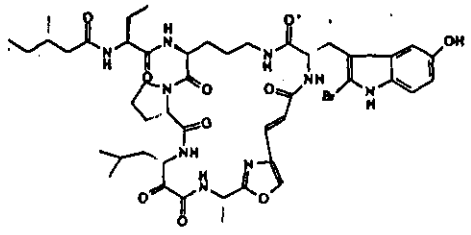
[208] bistratamide C



[209] bistratamide D



[210] cyclotheonamide A, R = CHO
[211] cyclotheonamide B, R = $OCOCH_3$



[212] orbiculamide A

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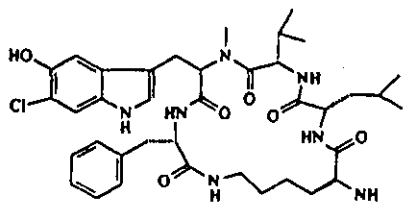
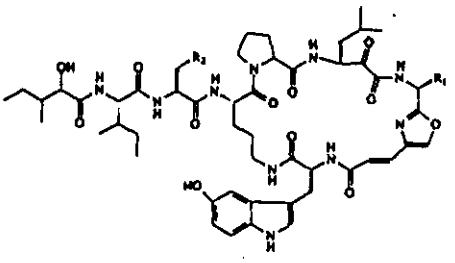
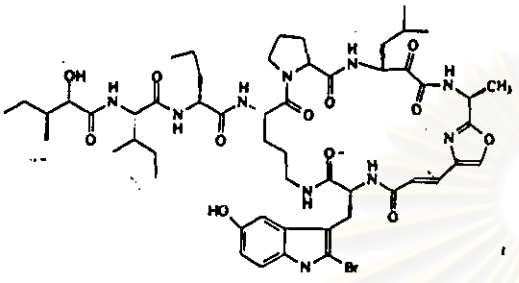


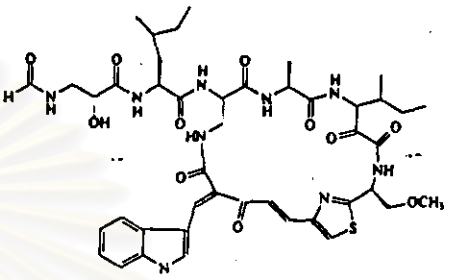
[213] kabiramide A



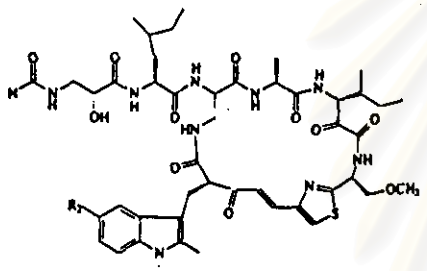
[214] kabiramide B, $R_1 = R_2 = CH_2CH_3$
[215] kabiramide C, $R_1 = CH_2CH_3$, $R_2 = CH_3$
[216] kabiramide D, $R_1 = R_2 = CH_3$



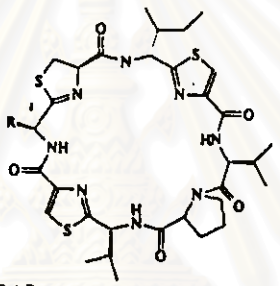
[217] keramamide E



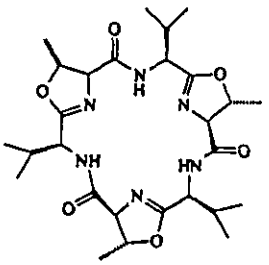
[218] keramamide G



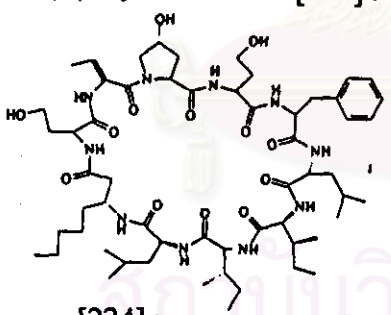
[219] keramamide H, $R_1 = Br$, $R_2 = OH$
[220] keramamide J, $R_1 = R_2 = H$



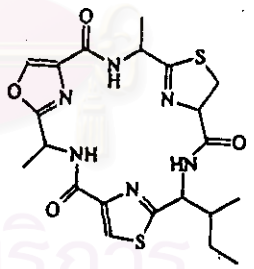
[221] tawicyclamide A, $R = -CH_2C_6H_5$
[222] tawicyclamide B, $R = -CH_2CH(CH_3)_2$



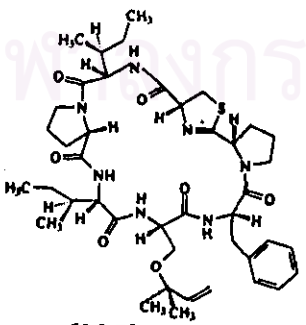
[223]
westiellamide [cycloxazoline]



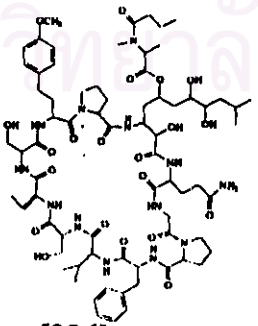
[224] hormothamnion A



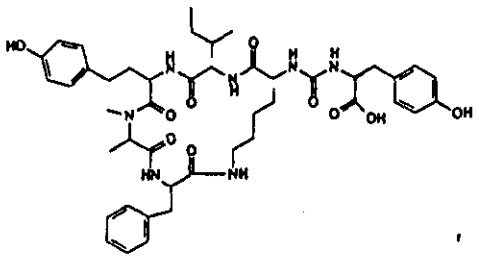
[227] dolastatin E



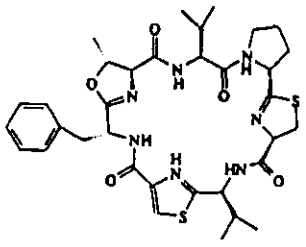
[225] mollamide



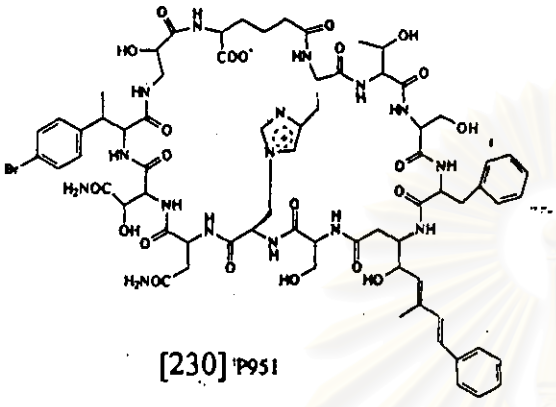
[226] schizotrin A



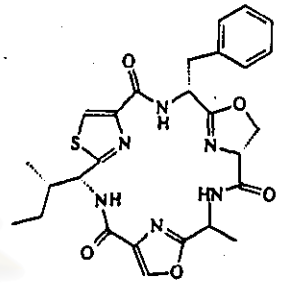
[228] oscillamide



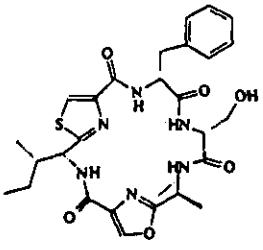
[229] cyclodidemnamide



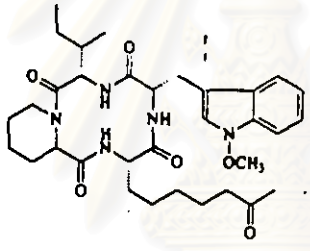
[230] P951



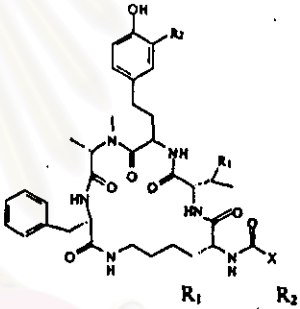
[231] raocyclamide A



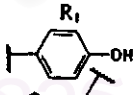
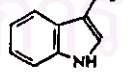
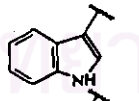
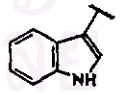
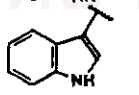
[232] raocyclamide A

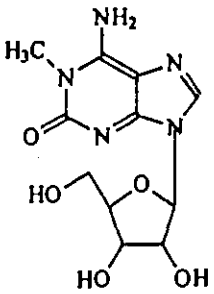


[233] apicidin

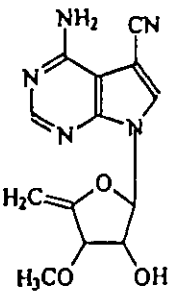


| | $R_1$ | $R_2$ | x |
|---|---|---|---|
| [234] anabaenopeptin B | $CH_3$ | H | Arg |
| [235] anabaenopeptin E | $CH_3$ | $CH_3$ | Arg |
| [236] anabaenopeptin F | $CH_2CH_3$ | H | Arg |

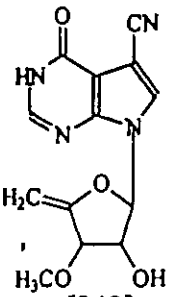
| | $R_1$ | $R_2$ | X |
|---|---|---|---|
| [237] loloatin A |  |  | H |
| [238] loloatin B |  |  | H |
| [239] loloatin C |  |  | H |
| [240] loloatin D |  |  | OH |



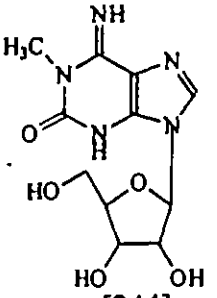
[241]
1-methylisoguanosine



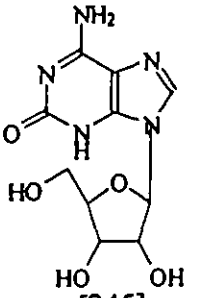
[242]
mycalisine A



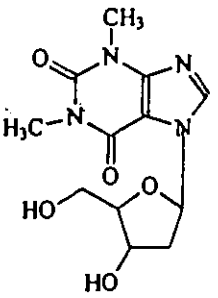
[243]
mycalisine B



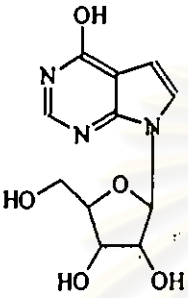
[244]
doridosine



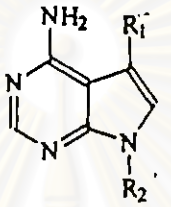
[245]
isoguanosine



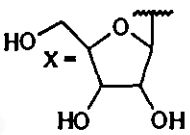
[246]
aplysidin



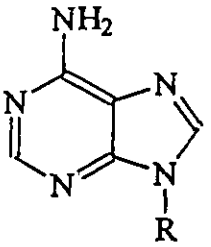
[247]
7-deazainosine



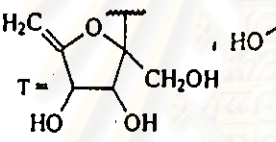
[248-251]

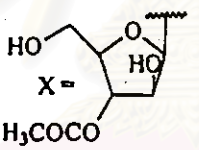


| Compounds | $R_1$ | $R_2$ |
|---|---|---|
| [248] tubercidin | H | X |
| [249] 5-iodo-5'-deoxytubercidin | I | Y |
| [250] 5'deoxy-3-bromotubercidin | Br | Y |
| [251] 5'deoxytubercidin | H | Y |

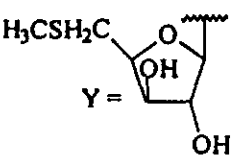


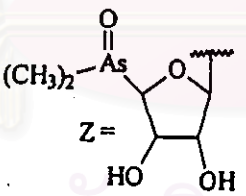
[252-258]

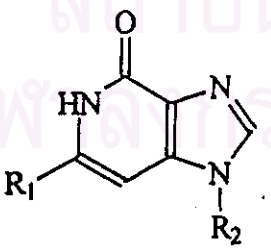




| Compounds | R |
|---|---|
| [252] augustmycin | T |
| [253] aristeromycin | U |
| [254] adenosine | V |
| [255] 9-β-D-arabinofuranosyladenine | W |
| [256] 3'-*O*-acetyl-9-β-D-arabinofuranosyladenine | X |
| [257] 9-[5'-deoxy-5'-(methylthio)-β-D-xylofuranosyl]adenine | Y |
| [258] 5'-deoxy-5'-dimethylarsinyladenosine | Z |







[259-262]

| Compounds | $R_1$ | $R_2$ |
|---|---|---|
| [259] 2'-deoxyguanosine | $NH_2$ | X |
| [260] 2'-deoxyinosine | H | X |
| [261] trachycladine A | Cl | Y |
| [262] trachycladine B | H | Y |