Issue 4, 2006

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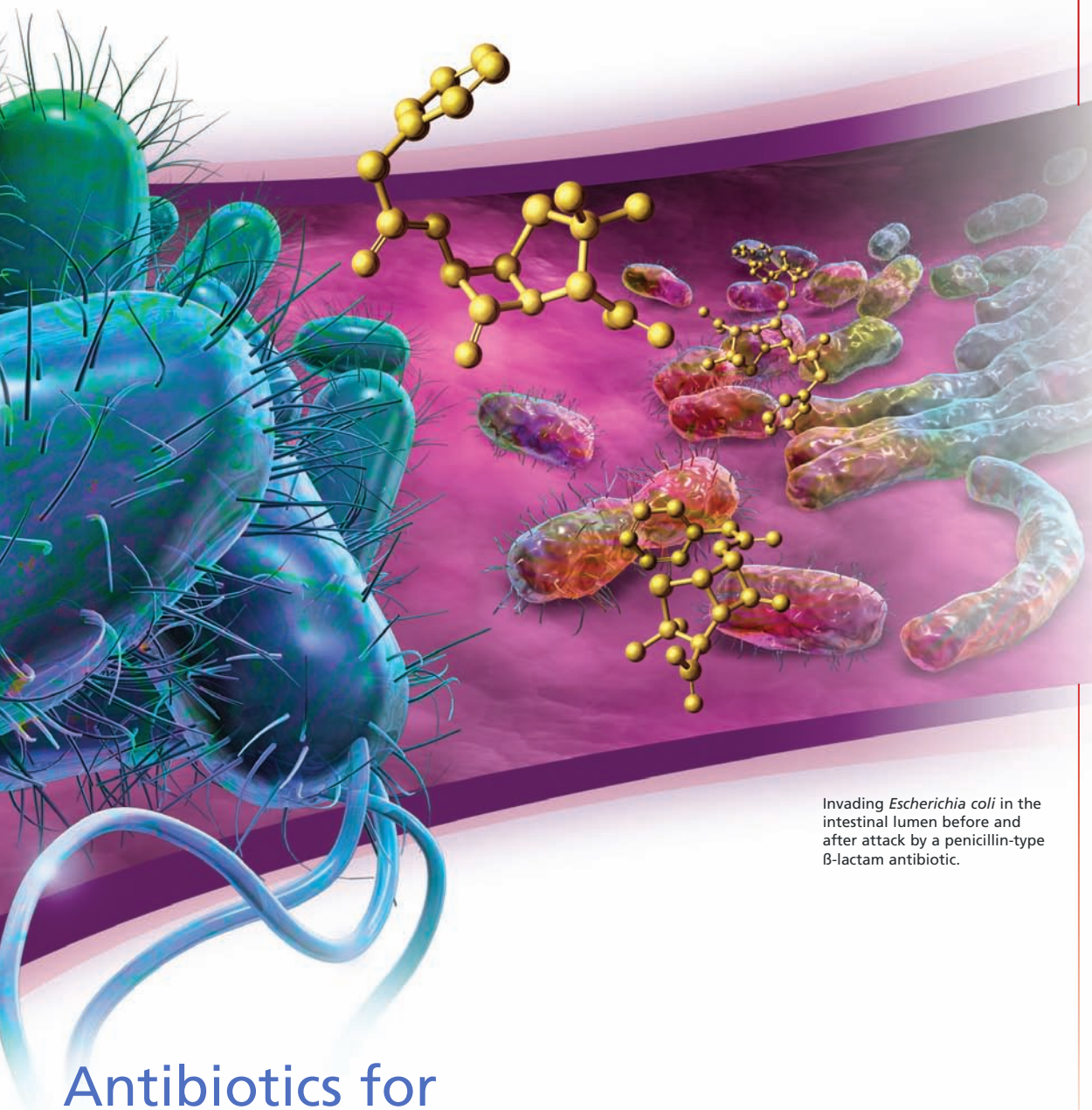

RECENT ADDITIONS
- Antineoplastic and Immunosuppressive Antibiotics
- Antibacterials
- Antifungals
- Antivirals

READY MADE ANTIBIOTIC SOLUTIONS

ANTIBIOTICS FOR PLANT TISSUE CULTURE

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Antibiotics for Research Applications

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Antibiotics for Research Applications

Introduction

The efficacy of natural antibiotics found in molds and plants had been known for centuries before the compounds themselves were isolated. Scientists began to have success identifying the active biochemicals found in antibacterial molds in 1928, with the rediscovery of penicillin by Fleming, identification of the chemical structure by Hodgkin, and subsequent synthesis by Chain, Heatley, and Florey, which led to commercial production of penicillin in the mid 1940's. Since then, researchers have not only discovered numerous natural antibacterial, antifungal and antiviral compounds, but also determined the critical cell mechanisms that are inhibited or blocked by these compounds. The understanding of these cellular activities has allowed for the development of subsequent generations of semisynthetic and synthetic antibiotics. The greatest impact of the identification and manufacture of antibiotics has clearly been in the area of human health. Scientists have been able to adapt these compounds for use in research and production applications to eliminate undesired bacteria, especially in cell culture. Some bacterial strains have evolved to develop resistance to specific antibiotics by enzymatic modification or degradation of the antibiotic, by modification of the drug target, or by exportation of the antibiotic through membrane efflux pumps. Geneticists have been able to exploit this trait by locating gene sequences that confer resistance and subsequently incorporating the resistance sequence into a plasmid that allows antibiotic selection of microorganisms transformed for recombinant protein expression.

This issue of BioFiles is designed to showcase selected antibiotics from a variety of Sigma-Aldrich's scientific areas. These fields, which include cell signaling, plant biotechnology, and cancer research, are not always associated with other research areas and techniques like cell culture and proteomics. However, antibiotics are universally used within life sciences to eliminate contamination and for study of the mechanisms used by bacteria and other cells to combat resistance, with the goal of developing new antibacterial and antineoplastic compounds.

Recent Additions

The following antibiotic products have been added since 2005. Sigma-Aldrich continues to expand our offerings of antibacterial, antiviral, antifungal, and antineoplastic chemicals in order to support your research. We welcome your recommendations for new products, whether antibiotics or other biochemicals. Please tell us your suggestions by visiting **sigma-aldrich.com/product_suggestions** or contact your local Sigma-Aldrich office.

Antineoplastic and Immunosuppresive Antibiotics

17-(Allylamino)-17-demethoxygeldanamycin

17-AAG; 17-(Allylamino)geldanamycin; CP 127374; 17-Demethoxy-17-allylamino-geldanamycin; Geldanamycin,17-demethoxy-17-(2-propenylamino)-; NSC 330507

$C_{31}H_{43}N_3O_8$ FW 585.69 [75747-14-7]

≥98% (HPLC)

Potent inhibitor of heat shock protein 90 (Hsp90). 17-AAG is a less toxic analog of geldanamycin. It induces apoptosis and displays anti-tumor effects. 17-AAG inhibits the activity of oncogenic proteins such as N-ras, Ki-ras, c-Akt, and $p185^{erB2}$.

solubility

DMSO ..... soluble
methanol ..... soluble

Ref: 1. Basso, A.D., et al., *Oncogene* **21**, 1159-1166 (2002)
2. Clarke, P.A., et al., *Oncogene* **19**, 4125-4133 (2000)
3. Nimmanapalli, R., et al., *Cancer Res.* **61**, 1799-1804 (2001)
4. Schnur, R.C., et al., *J. Med. Chem.* **38**, 3806-3812 (1995)

S: 22-24/25 -20°C WET ICE

A8476-500UG	500 µg

Cephalomannine

$C_{45}H_{53}NO_{14}$ FW 831.90 [71610-00-9]

≥97% (HPLC)

Antitumor; antiproliferative.

solubility

DMSO ..... 14 mg/mL

C4991-1MG	1 mg
C4991-5MG	5 mg

Chrysomycin A

$C_{28}H_{28}O_9$ FW 508.52 [82196-88-1]

≥98% (HPLC)

Antibiotic from *Streptomyces* sp. Inhibits the catalytic activity of human topoisomerase II. Exhibits antitumor activity against human cell lines K562, HT29, MCF7, PC6, and MKN28.

solubility

DMF ..... soluble
DMSO ..... soluble
ethanol ..... moderately soluble
methanol ..... moderately soluble

Ref: 1. Lorico, A., and Long, B.H., Biochemical characterization of elsamicin and other coumarin-related antitumor agents as potent inhibitors of human topoisomerase II. *Eur. J. Cancer* **29A**, 1985-1991 (1993)

2-8°C

C6616-100UG	100 µg

Chrysomycin B

$C_{27}H_{28}O_9$ FW 496.51 [83852-56-6]

≥98% (HPLC)

Antibiotic from *Streptomyces* sp. Inhibits the catalytic activity of human topoisomerase II. Exhibits antitumor activity against human cell lines K562, HT29, MCF7, PC6, and MKN28.

solubility

DMF ..... soluble
DMSO ..... soluble
ethanol ..... moderately soluble
methanol ..... moderately soluble

Ref: 1. Lorico, A., and Long, B.H., Biochemical characterization of elsamicin and other coumarin-related antitumor agents as potent inhibitors of human topoisomerase II. *Eur. J. Cancer* **29A**, 1985-1991 (1993)

2-8°C

C6491-100UG	100 µg

17-DMAG

17-Dimethylaminoethylamino-17-demethoxygeldanamycin

$C_{32}H_{48}N_4O_8$ FW 616.75

17-DMAG is a more potent water soluble analog of geldanamycin. Inhibits cancer growth and promotes apoptosis in multiple cell lines. 17-DMAG has shown more antitumor activity than 17-AAG.

solubility

DMSO ..... >25 mg/mL
ethanol ..... ~10 mg/mL

Ref: 1. Bull, E. E., et. al., *Clin. Cancer Res.* **10**, 8077-8074 (2004)
2. Kamal, A., et. al., *Trends Mol. Med.* **10**, 283-290 (2004)
3. Gossett, D. R., et. al., *Gynecol. Oncol.* **96**, 381 (2005)
4. Smith, V., et. al., *Eur. J. Cancer* **38**, S60 (2002)

-20°C

D5193-1MG	1 mg

Embelin

2,5-Dihydroxy-3-undecyl-2,5-cyclohexadiene-1,4-dione

$C_{17}H_{26}O_4$ FW 294.39 [550-24-3]

≥97% (HPLC)

Inhibitor of XIAP (X-linked inhibitor-of-apoptosis protein); *in vivo* antitumor and anti-inflammatory activity.

solubility

H_2O ..... insoluble
DMSO ..... 17 mg/mL

Ref: 1. Nikolovska-Coleska, Z., et al., Discovery of embelin as a cell-permeable, small-molecular weight inhibitor of XIAP through structure-based computational screening of a traditional herbal medicine three-dimensional structure database. *J. Med. Chem.* **47**, 2430-2440 (2004)
2. Chitra, M., et al., Antitumor, anti-inflammatory and analgesic property of embelin, a plant product. *Chemotherapy* **40**, 109-113 (1994)

EC No. 208-979-8 RTECS # DK4230000

E1406-10MG	10 mg
E1406-50MG	50 mg

Honokiol

5,3′-Diallyl-2,4′-dihydroxybiphenyl

$C_{18}H_{18}O_2$ FW 266.33 [35354-74-6]

≥98% (HPLC)

Natural biphenyl neolignan from magnolia extract; antiangiogenic; antitumor; anxiolytic.

solubility

H_2O ..... insoluble
DMSO ..... 36 mg/mL

R: 41-51/53 S: 26-39-61 2-8°C

H4914-10MG	10 mg
H4914-25MG	25 mg

ICRF-193

meso-4,4'-(3,2-Butanediyl)-bis(2,6-piperazinedione)
$C_{12}H_{18}N_4O_4$ FW 282.30 [21416-68-2]
≥95%
ICRF-193 induces a G_2 checkpoint that is associated with an ATR-dependent inhibition of polo-like kinase 1 (plk1) activity and a decrease in cyclin B1 phosphorylation.[1] Induces apoptosis in several cell lines including K562 and Molt-4 cells.[2,3] ICRF-193 is a topoisomerase II inhibitor that targets topoisomerase II_β to a greater extent than it targets topoisomeraseII_α[4] and does not cause DNA damage.[4]
solubility
DMSO ..... 4 mg/mL
Lit. cited: 1. Deming, P. et. al., *J. Biol. Chem.* **277**, 36832 (2002)
2. Hasinoff, B. et. al., *Mol. Pharmacol.* **59**, 453 (2001)
3. Iguchi, K. et. al., *Biochem. Pharmacol.* **57**, 1105 (1999)
4. Huang, K.C. et.al., *J. Biol. Chem.* **276**, 44488-44494 (2001)
R: 22-43 S: 36/37 RTECS # TL6380200 -20°C

I4659-1MG	1 mg
I4659-5MG	5 mg

Irinotecan hydrochloride

[1,4'-Bipiperidine]-1'-carboxylic acid; CPT-11; (*S*)-4,11-Diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester
$C_{33}H_{38}N_4O_6 \cdot HCl$ FW 623.14 [100286-90-6]
Antitumor agent. DNA topoisomerase inhibitor.
Ref: 1. Saijo, N, Preclinical and clinical trials of topoisomerase inhibitors. *Ann. N. Y. Acad. Sci.* **922**, 92 (2000)
2. Khayat, D., et al., The role of irinotecan and oxaliplatin in the treatment of advanced colorectal cancer. *Oncology* **15**, 415 (2001)
R: 22 RTECS # DW1061000 2-8°C

I1406-50MG	50 mg
I1406-250MG	250 mg

K-252a

$C_{27}H_{21}N_3O_5$ FW 467.47 [99533-80-9]
from *Nonomuraea longicatena*, ≥98% (HPLC)
Potent inhibitor of various protein kinases including protein kinase A, C, and G.
solubility
DMSO ..... 1 mg/mL
DMF ..... 1 mg/mL
RTECS # NZ0550000 -20°C DRY ICE

K1639-100UG	100 µg

Kazusamycin A

$C_{33}H_{48}O_7$ FW 556.73 [92090-94-3]
from *Streptomyces* sp., ≥95% (HPLC), aqueous methanol solution
Kazusamycin A, an unsaturated, branched-chain fatty acid with a terminal lactone ring, is a hydroxy analog of Leptomycin B. It has significant *in vitro* cytotoxic activity against various human and mouse tumor lines encompassing a wide range of tissue types. Kazusamycin A exhibits *in vivo* antitumor activity against experimental murine tumors. It inhibits nuclear export and Rev translocation, a regulatory gene product in the HIV genome, at nanomolar concentrations.
70% methanol solution.
solubility
methanol ..... soluble
DMSO ..... soluble
ethanol ..... soluble
chloroform ..... soluble
hexane ..... insoluble
H_2O ..... insoluble
methanol/water ..... 7:3, soluble
Ref: 1. Komiyama, K., et al., *Antibiotics* **38**, 220-223 (1985)
2. Roberts, B.J., et al., *Cancer Chemother. Pharmacol.* **16**, 95-101 (1986)
3. Komiyama, K., et al., *J. Antibiot.* **38**, 224-229 (1985)
4. Yoshida, E., et al., *J. Antibiot.* **40**, 391-393 (1987)
5. Wang, Y., et al., *Helv. Chim. Acta* **80**, 2157-2167 (1997)
R: 11-23/24/25-39/23/24/25 S: 7-16-36/37-45 Fp: 16 °C (60 °F) -20°C DRY ICE

K1764-1UG	1 µg

Magnolol

5,5′-Diallyl-2,2′-biphenyldiol
$C_{18}H_{18}O_2$ FW 266.33 [528-43-8]
≥98% (HPLC)
Bioactive plant component with antifungal,[1] antibacterial[2], and antioxidant effects.[3] Magnolol also demonstrates anti-inflammatory activity by interferring with NF-κB signaling.[4]
Lit. cited: 1. Bang, K.H., et al., Antifungal activity of magnolol and honokiol. *Arch. Pharm. Res.* **23**, 46-9 (2000)
2. Ho., K.Y., et al., Antimicrobial activity of honokiol and magnolol isolated from *Magnolia officinalis*. *Phytother Res.* **15**, 139-41 (2001)
3. Lo, Y.C., et al., Magnolol and honokiol isolated from *Magnolia officinalis* protect rat heart mitochondria against lipid peroxidation. *Biochem. Pharmacol.* **47**, 549-53 (1994)
4. Lee, J., et al., Anti-inflammatory effects of magnolol and honokiol are mediated through inhibition of the downstream pathway of MEKK-1 in NF-κB activation signaling. *Planta Med.* **71**, 338-43 (2005)
2-8°C

M3445-10MG	10 mg

Neocarzinostatin from *Streptomyces carzinostaticus*

Holoneocarzinostatin; NCS; NSC-69856; Zinostatin
[9014-02-2]
≥90% (SDS-PAGE), ~0.5 mg/mL
Neocarzinostatin is a protein-small molecule complex composed of an enediyne chromophore tightly bound to a 113-amino acid single chain protein. The complex possesses antiproliferative and antitumor activity. The chromophore is the active compound, which is responsible for DNA cleavage; while the apoprotein stabilizes and regulates the availability of the labile chromophore. NCS chromophore is bound non-covalently in a cleft of the binding protein and is dissociable. Upon addition of a thiol, the chromophore forms a highly reactive biradical species that can induce sequence-specific single and double strand breaks in DNA. Neocarzinostatin inhibits DNA synthesis and possesses antitumor activity in various human and animal tumors. NCS inhibits cellular proliferation by inducing G_2 cell cycle arrest and apoptosis in both human papilloma virus (HPV) positive and negative cell lines.

Solution in 20 mM MES buffer, pH 5.5.
Ref: 1. Tanoue, S., et al., Neocarzinostatin-chromophore: a potent inhibitor of casein kinase II *in vitro*. *Antibiotics* **51**, 95-98 (1998)
2. Heyd, B., et al., Reinvestigation of the proteolytic activity of neocarzinostatin. *J. Bacteriol.* **182**, 1812-1818 (2000)
3. Smith, A.L., and Nicolaou, K.C., The enediyne antibiotics. *J. Med. Chem.* **39**, 2103-2117 (1996)
2-8°C WET ICE

N9162-100UG	100 µg

Antineoplastic and Immunosuppresive Antibiotics

Reveromycin A

$C_{36}H_{52}O_{11}$ FW 660.79 [134615-37-5]
≥98% (HPLC)
Polyketide antibiotic from *Streptomyces* sp. Epidermal growth factor (EGF) inhibitor; apoptosis inducer; G_1 phase cell cycle inhibitor having antiproliferative behavior against human cell lines KB and K562 as well as antifungal activity.
solubility
ethyl acetate ..... soluble
ethanol ..... soluble
methanol ..... soluble
DMF ..... soluble
DMSO ..... soluble
Ref: 1. Miyamoto, Y., et al., Identification of *Saccharomyces cerevisiae* isoleucyl-tRNA synthetase as a target of the G1-specific inhibitor Reveromycin A. *J. Biol. Chem.* **277**, 28810 (2002)
2. Tanaka, Y., et al., Reveromycin A inhibits antigen receptor-mediated antigen presentation by B lymphoma cells via its effect on intracellular trafficking of the antigen. *J. Antibiot. (Tokyo)* **55**, 28810-28814 (2002)
3. Takahashi, H., et al., Reveromycins, new inhibitors of eukaryotic cell growth. II. Biological activities. *J. Antibiot. (Tokyo)* **45**, 1414-1419 (1992)
4. Takahashi, H., et al., Reveromycins, new inhibitors of eukaryotic cell growth. I. Producing organism, fermentation, isolation and physico-chemical properties. *J. Antibiot. (Tokyo)* **45**, 1409-1413 (1992)
-20°C WET ICE

R0654-100UG	100 µg

Antibacterials

Borrelidin

Borrelidine; 2-(7-Cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl)-cyclopentanecarboxylic acid; NSC 216128; Treponemycin
$C_{28}H_{43}NO_6$ FW 489.64 [7184-60-3]
Borrelidin, an 18-membered macrolide-polyketide, is a compound with antiviral, antibacterial, antimalarial, and antiangiogenic properties. It is a known inhibitor of bacterial and eukaryotic threonyl-tRNA synthetases. Borrelidin induces apoptosis in endothelial cells via the caspase 3 and caspase 8 pathway. In addition, borrelidin strongly inhibits capillary tube formation and also disrupts formed capillary tubes by inducing apoptosis of the tube-forming cells in a rat aorta matrix culture model. In *S. cerevisiae,* borrelidin inhibits the cyclin-dependent kinase Cdc28/Cln2 with an IC_{50} of 24 µM, causing the arrest of both haploid and diploid cells in G_1 phase and inducing the transcription of amino acid biosynthetic enzymes through a *GCN4*-dependent pathway.
Ref: 1. Ruan, B., et al., A unique hydrophobic cluster near the active site contributes to differences in borrelidin inhibition among threonyl-tRNA synthetases. *J. Biol. Chem.* **280**, 571-577 (2005)
2. Kawamura, T., et al., Anti-angiogenesis effects of borrelidin are mediated through distinct pathways: threonyl-tRNA synthetase and caspases are independently involved in suppression of proliferation and induction of apoptosis in endothelial cells. *J. Antibiot. (Tokyo)* **56**, 709-715 (2003)
3. Vong, B.G., et al., Stereoselective total synthesis of (-)-borrelidin. *Angew. Chem. Int. Ed. Engl.* **43**, 3947-3951 (2004)
RTECS # ED8750000

▸ **from *Streptomyces* sp., ≥95% (HPLC)**
solubility
ethyl acetate ..... soluble
ethanol ..... soluble
methanol ..... soluble
DMF ..... soluble
DMSO ..... soluble
2-8°C

B1936-100UG	100 µg

▸ **from *Streptomyces parvulus*, ≥98% (HPLC)**
solubility
DMSO ..... 1 mg/mL
methanol ..... 1 mg/mL
-20°C WET ICE

B3061-1MG	1 mg

Chrysomycin A, see under Antineoplastic and Immunosuppresive Antibiotics *Page* 2
Chrysomycin B, see under Antineoplastic and Immunosuppresive Antibiotics *Page* 2

Elafin

Human, recombinent, expressed in *Saccharomyces cerevisiae*, >90% (by MS, HPLC and SDS-PAGE)
Inhibitor of human leukocyte elastase and proteinase 3. May protect certain tissues against destruction by the immune system.
R: 22-36/37/38 S: 26-36 -20°C

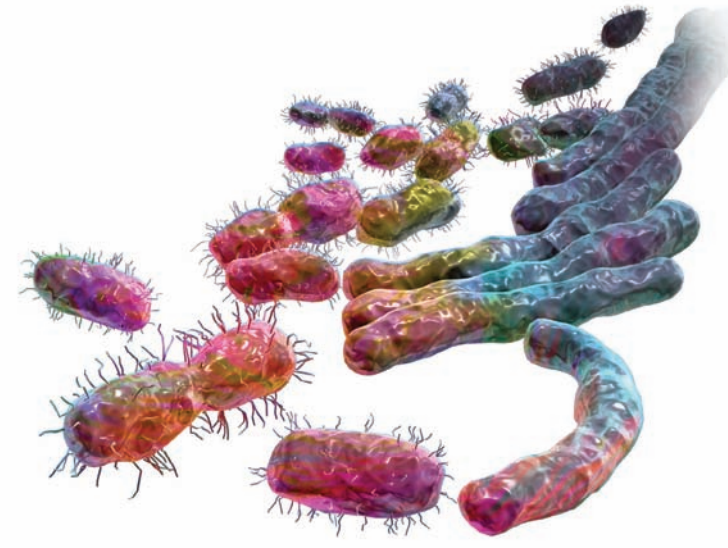
E7280-100UG	100 µg

Honokiol, see under Antineoplastic and Immunosuppresive Antibiotics *Page* 2
Magnolol, see under Antineoplastic and Immunosuppresive Antibiotics *Page* 3

Mupirocin

5,9-Anhydro-2,3,4,8-tetradeoxy-8-[[3-(2-hydroxy-1-methylpropyl)oxiranyl]methyl]-3-methyl-[2E,8[2S,3S(1S,2S)]]-L-talonon-2-enonic acid 8-carboxy-octyl ester; BRL 4910A; Pseudomonic acid
$C_{26}H_{44}O_9$ FW 500.62 [12650-69-0]
≥94% (HPLC)
Antibiotic; inhibits isoleucyl-tRNA synthetase (IRS).
solubility
H_2O ..... 12 mg/mL
RTECS # RA6907000

M7694-50MG	50 mg
M7694-100MG	100 mg



Antifungals

Aculeacin A

$C_{50}H_{81}N_7O_{16}$ FW 1036.22 [58814-86-1]

from *Aspergillus aculeatus*, ≥95% (HPLC)

Aculeacin A, an amphophilic antibiotic, inhibits the biosynthesis of β–glucan by selective blockage of β(1→3) glucan synthase.

solubility

methanol	soluble
ethanol	soluble
DMF	soluble
DMSO	10 mg/mL

Ref: 1. Takeshima, H., et al., *J. Biochem.* **105**, 606 (1989)
2. Yamaguchi, H., et al., *Microbiol. Immunol.* **29**, 609 (1985)
3. Mizuno, K., et al., *J. Antibiot.* **30**, 297 (1977)

RTECS # AU2980000 –20°C WET ICE

A7603-1MG	1 mg

Cinnamycin

Ro 09-0198

Cys-Arg-Gln-Cys-Cys–3-NH_2-Ala-Phe-Gly-Pro-Phe-(2*S*,3*S*)-2-amino-3-mercaptobutanoyl-Phe-Val-Cys-3-OH-α-Asp-Gly-Asn-(2*S*,3*S*)-2-amino-3-mercaptobutanoyl-Lys (Disulfide bridges: 1-18, 4-14, 5-11; Lysinoalanine bridge: 6-19)

$C_{89}H_{125}N_{25}O_{25}S_3$ FW 2041.29 [110655-58-8]

≥90% (HPLC)

Cinnamycin (Ro 09-0198) is a tetracylic peptide antibiotic (19 amino acids) that binds specifically to the cell surface phosphatidylethanolamine and subsequently induces cytolysis. This is a rare example of a small peptide binding to a particular lipid (1:1 complex). Cinnamycin belongs to the duramycin-type lantibiotics and contains the unusual thioether lanthionine amino acids.

solubility

methanol and water	5 mg/mL
acetonitrile:water	5 mg/mL

Ref: 1. Machiadze, G., et al., Specific binding of Ro 09-0198 (cinnamycin) to phosphatidylethanolamine: a thermodynamic analysis. *Biochemistry* **41**, 1965-1971 (2002)
2. Widdick, D. A. et al., Cloning and engineering of the cinnamycin biosynthetic gene cluster from *Streptomyces cinnamoneus cinnamoneus* DSM 40005 *Proc. Natl. Acad. Sci. USA* **100**, 4316-4321 (2003)

S: 22-24/25 RTECS # GE1745000 ◆ 2-8°C

C5241-1MG	1 mg

Fumitremorgin C

FTC

$C_{22}H_{25}N_3O_3$ FW 379.45 [118974-02-0]

from *Neosartorya fischeri*, >98% (HPLC and TLC)

Fumitremorgin C (FTC) is a fungal toxin of the diketopiperazines family of compounds. In mammalian cells, FTC is tremorgenic and causes cell cycle arrest. FTC has been shown to reverse resistance to doxorubicin, mitoxantrane, and topotecan in non-Pgp (P-glycoprotein), non-MRP (multidrug resistance protein) multidrug-resistance (MDR) cells. This reversal of resistance is associated with an increase in drug accumulation. FTC is a specific, selective, and potent inhibitor at micromolar concentrations of the breast cancer resistant protein (BCRP/ABCG2), an ABC transporter associated with chemotherapy resistance. FTC, in combination with mitoxantrone, can be used for the detection of ABCG2 functional activity in several cell lines.

solubility

DMSO	soluble
chloroform	soluble
methanol	5 mg/mL
acetonitrile	5 mg/mL

Ref: 1. Van Loevezijn, A., et al., Inhibition of BCRP-mediated drug efflux by fumitremorgin-type indolyl diketopiperazines. *Bioorg. Med. Chem. Lett.* **11**, 29-32 (2001)
2. Rabindran, S.K., et al., Fumitremorgin C reverses multidrug resistance in cells transfected with the breast cancer resistance protein. *Cancer Res.* **60**, 47-50 (2000)
3. Cui, C.B., et al., Novel mammalian cell cycle inhibitors, tryprostatins A, B, and other diketopiperazines produced by *Aspergillus fumigatus*. I. Taxonomy, fermentation, isolation, and biological properties. *J. Antibiot.* **49**, 527-533 (1996)
4. Rabindran, S.K., et al., Reversal of a novel multidrug resistance mechanism in human colon carcinoma cells by fumitremorgin C. *Cancer Res.* **58**, 5850-5858 (1998)
5. Minderman, H., et al., Flow cytometric analysis of breast cancer resistance protein expression and function. *Cytometry* **48**, 59-65 (2002)

S: 22-24/25 ◆ 2-8°C WET ICE

F9054-250UG	250 µg

Leptomycin A

19-(3,6-Dihydro-3-methyl-6-oxo-2H-pyran-2-yl)-3,5,7,9,11,15,17-heptamethyl-6-hydroxy-8-oxo-2,10,12,16,18-nonadecapentaenoic acid; Jildamycin

$C_{32}H_{46}O_6$ FW 526.70 [87081-36-5]

from *Streptomyces* sp., ~95% (HPLC), methanol solution

Leptomycins are antifungal antibiotics with unique unsaturated, branched-chain fatty acid structures.[1] The physiochemical and biological properties of Leptomycins A and B are very similar.[2] Both are considered to be specific inhibitors of nuclear export. The suggested inhibition mechanism involves the direct binding of leptomycins to CRM1 (Exportin-1), which is the main nuclear export protein. This blocks the binding of CRM1 to proteins containing a nuclear export signal (NES),[3,4] and thus prevents their export from the nucleus. Although more research on nuclear export inhibition has been performed using Leptomycin B, it has been shown that Leptomycin A has similar effects and can induce, for example, nuclear accumulation of wild-type ERK5.[5]

Leptomycin A is also active against *Schizosaccaromyces pombe* and *Mucor rouxianus*.[2]

Lit. cited: 1. Hamamoto, T., et al., *J. Antibiot.* **38**, 533-535 (1985)
2. Hamamoto, T., et al., *J. Antibiot.* **36**, 636-645 (1983)
3. Nishi, K., et al., *J. Biol. Chem.* **269**, 6320-6324 (1994)
4. Henderson, B.R., and Eleftheriou, A., *Exp. Cell Res.* **256**, 213-224 (2000)
5. Buschbeck, M., and Ullrich, A., *J. Biol. Chem.* **280**, 2659-2667 (2005)

R: 11-23/24/25-39/23/24/25 S: 7-16-36/37-45 ◆ –20°C DRY ICE

L6417-1UG	1 µg

Magnolol, see under Antineoplastic and Immunosuppresive Antibiotics *Page* 3
Reveromycin A, see under Antineoplastic and Immunosuppresive Antibiotics *Page 4*

Antifungals

Sordarin sodium salt

$C_{27}H_{39}NaO_8$ FW 514.58 [463356-00-5]
from *Sordaria araneosa*, ≥98% (HPLC)
Sordarin is an antifungal metabolite possessing a tetracyclic diterpene glycoside structure. It is a highly potent inhibitor of eukaryotic protein synthesis with selectivity for the fungal translation machinery. The elongation factor eEF-2 is the molecular target for sordarin. It blocks ribosomal translocation by stabilizing the EF2-ribosome complex in a manner similar to that of fusidic acid in the bacterial system. Additional cellular components (including rpP0, which is an essential protein of the ribosomal large subunit stalk) are involved in its mechanism of action. Sordarin inhibits *in vitro* translation in the pathogenic fungi *C. albicans*, *C. glabrata*, and *C. neoformans*. In addition to its therapeutic potential, sordarin is a useful tool for the analysis of protein translation events.
solubility
H_2O ..... ≤10 mg/mL
◆ -20°C WET ICE

S1442-5MG	5 mg

Thiolutin

Aureothricin; N-(4,5-Dihydro-4-methyl-5-oxo-1,2-dithiolo[4,3-B]pyrrol-6-yl); Farcinicin; Propiopyvothine
$C_8H_8N_2O_2S_2$ FW 228.29 [87-11-6]
from *Streptomyces luteosporeus*, ≥95% (HPLC)
Thiolutin is a sulfur-containing antibiotic, which is a potent inhibitor of bacterial and yeast RNA polymerases. It was found to inhibit *in vitro* RNA synthesis directed by all three yeast RNA polymerases (I, II, and III). Thiolutin is also an inhibitor of mannan and glucan formation in *Saccharomyces cerevisiae* and used for the analysis of mRNA stability. Studies have shown that thiolutin inhibits adhesion of human umbilical vein endothelial cells (HUVECs) to vitronectin and thus suppresses tumor cell-induced angiogenesis *in vivo*.
solubility
DMSO ..... 5 mg/mL
R: 28 S: 45 RTECS # JP1355000 -20°C WET ICE

T3450-1MG	1 mg

Venturicidin A

Aabomycin A_1
$C_{41}H_{67}NO_{11}$ FW 749.97 [33538-71-5]
from *Streptomyces* sp., ≥95% (HPLC)
Antifungal antibiotic; uncoupler of mitchondrial oxidative phosphorylation. F_0F_1-ATPase (ATP synthase) inhibitor.
solubility
ethanol ..... soluble
methanol ..... soluble
DMF ..... soluble
DMSO ..... soluble
Ref: 1. Matsuno-Yagi, A., and Hatefi, Y., Studies on the mechanism of oxidative phosphorylation. ATP synthesis by submitochondrial particles inhibited at F_0 by venturicidin and organotin compounds. *J. Biol. Chem.* **268**, 6168-6173 (1993)
EC No. 251-568-3 RTECS # YX4556000 2-8°C

V6264-100UG	100 µg

Antivirals

(-)-Arctigenin

(3*R*,4*R*)-4-[(3,4-Dimethoxyphenyl)methyl]dihydro-3-[(4-hydroxy-3-methoxyphenyl)methyl]-2(3H)-furanone
$C_{21}H_{24}O_6$ FW 372.41 [7770-78-7]
≥98% (HPLC)
Dibenzylbutyrolactone ligand, natural product, viral integrase and topoisomerase II inhibitor, antioxidant, antiviral, anti-inflammatory, immunomodulator.
solubility
DMSO ..... 34 mg/mL, soluble, with heating and sonicating
S: 22-24/25 -20°C

A1854-10MG	10 mg
A1854-25MG	25 mg

Borrelidin, see under Antibacterials *Page* 4
K-252a, see under Antineoplastic and Immunosuppresive Antibiotics *Page* 3

Matrine

Matridin-15-one ; Sophocarpidine
$C_{15}H_{24}N_2O$ FW 248.36
Matrine is an alkaloid that is one of the major components in the root of the saphoro plant. Matrine has been studied for possible antiviral efficacy against hepatitis B and C, as well as impact against some skin diseases and forms of cancer.
R: 22 S: 36/37 RTECS # OQ1754000 2-8°C

M5319-100MG	100 mg
M5319-500MG	500 mg

How Antibiotics Work

Antibiotics are molecules that specifically target and kill cells. The term antibiotic is frequently used interchangeably with the word antibacterial, but antiviral, antifungal and antineoplastic compounds are also classified as antibiotics. Antibacterial action generally falls within one of three mechanisms, which involve the inhibition or regulation of enzymes involved in cell wall biosynthesis, nucleic acid metabolism and repair, or protein synthesis, respectively. Many of these cellular functions targeted by antibiotics are most active in multiplying cells. Since there is often overlap in these functions between prokaryotic bacterial cells and eukaryotic mammalian cells, it is not surprising that some antibiotics have also been found to be useful as anticancer agents.

Inhibition of Cell Wall Biosynthesis

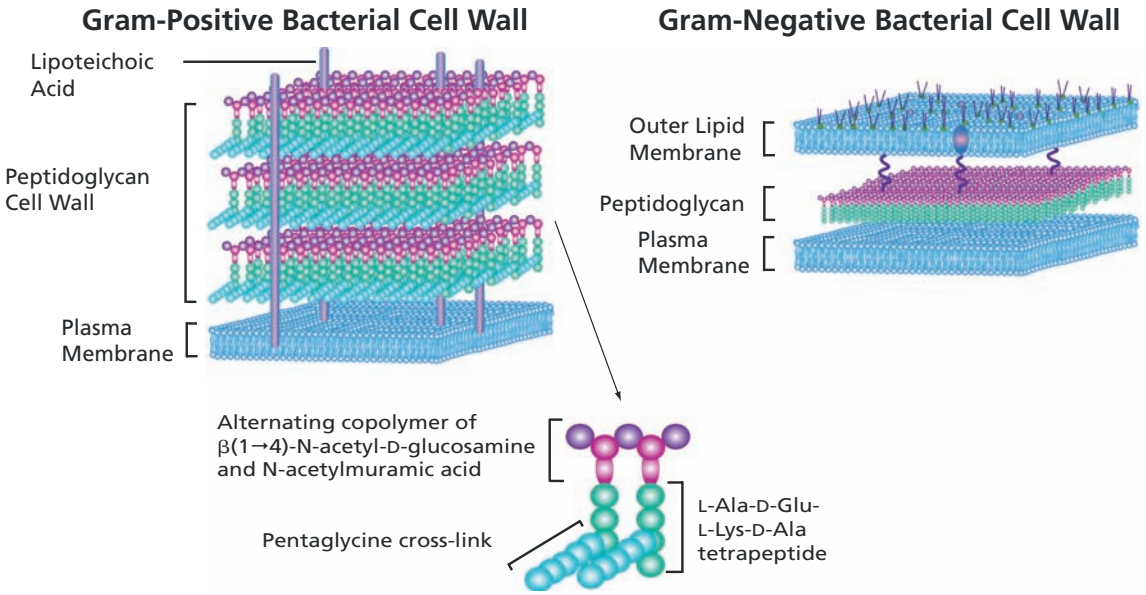
Structurally, bacteria resemble primitive plants in that the cellular contents are surrounded by an inner peptidoglycan cell wall in addition to an inner plasma membrane and, in Gram-negative bacteria, an outer lipid bilayer. Specific antibacterials interfere with the synthesis of the cell wall, weakening the peptidoglycan scaffold within the bacterial wall so that the structural integrity eventually fails. Since mammalian cells have a plasma membrane but lack the peptidoglycan wall structure, this class of antibacterials selectively targets the bacteria with no significant negative effect on the cells of the mammalian host.

Peptidoglycan construction begins in the cytoplasm with the synthesis of a muramyl peptapeptide precursor containing a terminal D-Ala-D-Ala. Some antibiotics interfere with the synthesis of the basic peptidoglycan building block. For example, **D-cycloserine** inhibits two enzymes involved in the precursor synthesis, preventing both conversion of L-alanine to D-alanine by racemase, and the construction of D-alanyl-D-alanine by D-Ala-D-Ala ligase. In the cytoplasm, muramyl pentapeptide is anchored via a water-soluble UDP-glucosamine moiety.

In the second phase of peptidoglycan construction, muramyl pentapeptide N-acetylglucosamine is transferred to a C_{55} undecaprenyl phosphate with the release of UMP to form a Lipid I intermediate. **Tunicamycin** inhibits the enzymatic conversion of the undecaprenyl phosphate to the lipid I intermediate, stopping the completion of the peptidoglycan structure. An additional glycosylation step completes the peptidoglycan unit, following which it is transported via its C_{55} lipid tail to the external periplasmic surface of the membrane where its peptidyglycan unit becomes integrated into the cell wall matrix. **Bacitracin** inhibits lipid phosphatase, preventing the release of the finished peptidoglycan from its C_{55} lipid carrier.

Several transpeptidases and transglycosylases connect the newly formed peptidoglycan structures to the cell wall peptidoglycan matrix. The specificity of β-lactam antibacterials is due to their ability to inhibit transpeptidase enzymes and prevent the assembly of the peptidoglycan layer in both Gram-positive and Gram-negative bacteria. β-Lactam molecules, with their structural similarity to the D-alanyl-D-alanine group within the peptidoglycan structure, compete for the binding sites of transpeptidases. When it was first commercialized, **penicillin**, a β-lactam antibiotic, was considered a "magic bullet" because of its specificity for bacterial infections without harming the patient.

Vancomycin, a glycopeptide antibiotic with a significantly larger structure, also prevents cell wall construction by interfering with transglycosylases. Its effectiveness is limited to Gram-positive bacteria because it is unable to penetrate the outer cytoplasmic membrane of Gram-negative bacteria due to its large size as compared to penicillin.



Inhibition of Cell Wall Biosynthesis

Bacitracin

$C_{66}H_{103}N_{17}O_{16}S$ FW 1422.69 [1405-87-4] EC No. 2157862
from *Bacillus licheniformis*, activity: ≥50,000 U/g
Peptide antibiotic.
Antimicrobial spectrum: Gram-positive bacteria.
Mode of Action: Inhibits bacterial cell wall synthesis by inhibiting dephosphorylation of lipid pyrophosphate.
S: 22-24/25 EC No. 215-786-2 Hygroscopic RTECS # CP0175000 2-8°C

B0125-50KU	50,000 units
B0125-250KU	250,000 units
B0125-1250KU	1,250,000 units

D-Cycloserine

(*R*)-4-Amino-3-isoxazolidone
$C_3H_6N_2O_2$ FW 102.09 [68-41-7] EC No. 2006884 BRN 80798
microbial
Antibiotic against Gram-negative bacteria that acts by inhibiting the synthesis of bacterial cell walls.
EC No. 200-688-4 RTECS # NY2975000 -20°C

C6880-1G	1 g
C6880-5G	5 g

Penicillin G sodium salt

Benzylpenicillin sodium salt
$C_{16}H_{17}N_2NaO_4S$ FW 356.37 [69-57-8] EC No. 2007102 BRN 3834217
activity: ~1650 units/mg
Mode of Action: Inhibits bacterial cell wall synthesis.
Antimicrobial spectrum: Gram-positive bacteria.
Ref: 1. Martin, H.H. and Gmeiner, J., Modification of peptidoglycan structure by penicillin action in cell walls of *Proteus mirabilis*. *Eur. J. Biochem.* **95**, 487 (1979)
R: 42/43 S: 22-36/37-45 EC No. 200-710-2 RTECS # XH9800000

PENNA-1MU	1,000,000 units
PENNA-10MU	10,000,000 units
PENNA-25MU	25,000,000 units
PENNA-100MU	100,000,000 units

Tunicamycin from *Streptomyces* sp.

[11089-65-9] BRN 6888090
Blocks the formation of protein N-glycosidic linkages by inhibiting the transfer of N-acetylglucosamine 1–phosphate to dolichol mono-phosphate.

Contains homologues A, B, C, and D. Composition may vary from lot to lot.
Ref: 1. Duksin, D. and Mahoney, W.C., Relationship of the structure and biological activity of the natural homologues of tunicamycin. *J. Biol. Chem.* **257**, 3105-3109 (1982)
2. Mahoney, W.C. and Duksin, D., Separation of tunicamycin homologues by reversed-phase high-performance liquid chromatography. *J. Chromatogr. Sci.* **198**, 506-510 (1980)
3. Matthies, H. Jr, et al., Glycosylation of proteins during a critical time window is necessary for the maintenance of long-term potentiation in the hippocampal CA1 region. *Neuroscience* **91**, 175-183 (1999)
4. Yunovitz, H., Gross, K.C., Effect of tunicamycin on metabolism of unconjugated N-glycans in relation to regulation of tomato fruit ripening. *Phytochemistry* **37**, 663-668 (1994)
5. Nishizaki ,T., Tunicamycin alters channel gating characteristics of junctional and extrajunctional acetylcholine receptors expressed in *Xenopus oocytes*. *Neuroscience* **170**, 273 (1994)
R: 28 S: 28-37/39-45 Light sensitive, Moisture sensitive RTECS # YO7980200 2-8°C

T7765-1MG	1 mg
T7765-5MG	5 mg
T7765-10MG	10 mg
T7765-50MG	50 mg

Vancomycin hydrochloride

$C_{66}H_{75}Cl_2N_9O_{24} \cdot HCl$ FW 1485.71 [1404-93-9] BRN 3704657
from *Streptomyces orientalis* potency, ≥900 μg per mg (as vancomycin base)
Glycopeptide antibiotic
Mode of action: Interferes with cell wall synthesis
Antimicrobial spectrum: Gram-positive bacteria
Studies on bond strength in vancomycin-peptide complexes;[1] Structure of vancomycin and its complex with acetyl-D-alanyl-D-alanine[2].
Lit. cited: 1. Williamson, M.P., and Williams, D.H., *Eur. J. Biochem.* **138**, 345 (1984)
2. Sheldrick, et al., *Nature* **271**, 223 (1978)
R: 43 S: 36/37 RTECS # YW4380000 2-8°C

V2002-100MG	100 mg
V2002-250MG	250 mg
V2002-1G	1 g
V2002-5G	5 g

Inhibition of Nucleic Acid Synthesis

Quinolones are a key group of antibiotics that interfere with DNA synthesis by inhibiting topoisomerase, most frequently topoisomerase II (DNA gyrase), an enzyme involved in DNA replication. DNA gyrase relaxes supercoiled DNA molecules and initiates transient breakages and rejoins phosphodiester bonds in superhelical turns of closed-circular DNA. This allows the DNA strand to be replicated by DNA or RNA polymerases. The fluoroquinolones, second-generation quinolones that include **levofloxacin**, **norfloxacin**, and ciprofloxacin, are active against both Gram-negative and Gram-positive bacteria.

Topoisomerases are present in both prokaryotic and eukaryotic cells, but the quinolones are specific inhibitors of bacterial topoisomerase II. Inhibitors that are effective against mammalian topoisomerases, such as **irinotecan** and etoposide, are used as antineoplastic drugs to kill cancer cells.

Rifampicin blocks initiation of RNA synthesis by specifically inhibiting bacterial RNA polymerase. It does not interact with mammalian RNA polymerases, making it specific for Gram-positive bacteria and some Gram-negative bacteria.

Some antibiotics that interfere with RNA synthesis by inhibiting RNA polymerase, such as **doxorubicin** and **actinomycin D (dactinomycin)**, are not specific for bacteria and interfere with both bacterial and mammalian systems. These are most often used as antineoplastic and antitumor drugs, attacking rapidly growing malignant cells as well as normal cells. Because cancerous cells are growing at a faster rate than surrounding normal tissue, a higher percentage of malignant cells are attacked by cytotoxic drugs. However, antitumor drugs cannot differentiate between malignant cells and fast-dividing normal cells such as those of the intestinal epithelium or hair follicles.

Actinomycin D

Actinomycin C_1; Actinomycin IV; Dactinomycin
$C_{62}H_{86}N_{12}O_{16}$ FW 1255.42 [50-76-0] EC No. 2000636 BRN 605235
from *Streptomyces* sp., ~98% (HPLC)
An antineoplastic antibiotic that inhibits cell proliferation by forming a stable complex with DNA and blocking the movement of RNA polymerase which interferes with DNA-dependent RNA synthesis. Induces apoptosis. Potent antitumor agent. For cell culture applications, actinomycin D is used as a selection agent and is used in banding techniques to differentiate between different regions of chromosomes.
solubility
ethanol ..... soluble
DMSO ..... 1 mg/mL
Ref: 1. Wadkins, R.M., Actinomycin D binding to single-stranded DNA: sequence specificity and hemi-intercalation model from fluorescence and 1H NMR spectroscopy. *J. Mol. Biol.* **262**, 53 (1996)
2. Glynn, J.M., et al., Apoptosis induced by Actinomycin D, Camptothecin or Aphidicolin can occur in all phases of the cell cycle. *Biochem. Soc. Trans.* **20**, 84S (1992)
R: 28 S: 22-28-36/37-45 EC No. 200-063-6 RTECS # AU1575000 2-8°C

A1410-2MG	2 mg
A1410-5MG	5 mg
A1410-10MG	10 mg
A1410-25MG	25 mg
A1410-50MG	50 mg
A1410-100MG	100 mg

Doxorubicin hydrochloride

Adriamycin hydrochloride; DOX; Hydroxydaunorubicin hydrochloride
$C_{27}H_{29}NO_{11} \cdot HCl$ FW 579.98 [25316-40-9] EC No. 2468183
BRN 4229251
~98% (TLC)
Naturally fluorescent anthracycline antibiotic, anticancer drug. Doxorubicin is a substrate of MRP1 which was first cloned from a DOX-resistant lung cancer cell line. Fluorescent property has been exploited for the measurement of drug efflux pump activities as well as resolving the important question of intracellular localization of various multidrug resistance proteins and the role of subcellular organelles (Golgi and lysosome) in the sequestration of drugs and its implication in drug resistant phenotypes.
Ref: 1. C.N. Ellis et al., *Biochem. J.* **245**, 309 (1987)
2. R.J. White et al., *Drugs Pharm. Sci.* **22**, 569 (1984)
3. A. Vigevani, M.J. Williamson, *Anal. Profiles Drug Subst.* **9**, 245 (1980)
4. Friesen, C., et al., Cytotoxic drugs and the CD95 pathway. *Leukemia* **13**, 1854 (1999)
5. Kraus-Berthier, L, et al., Histology and sensitivity to anticancer drugs of two human non-small cell lung carcinomas implanted in the pleural cavity of nude mice. Clin. *Cancer Res.* **6**, 297-304 (2000)
6. Sparano, J.A., Doxorubicin/taxane combinations: cardiac toxicity and pharmacokinetics. *Semin. Oncol.* **26**, 14-19 (1999)
7. Gong, Y., et al., *J. Biol. Chem.* **278**, 50234-50239 (2003)
8. Rajagopal, A., and Simon, S.M., *Mol. Biol. Cell.* **14**, 3389-3399 (2003)
R: 45-22 S: 53-45 EC No. 246-818-3 Light sensitive, Moisture sensitive
RTECS # QI9295900 2-8°C

D1515-10MG	10 mg

Irinotecan hydrochloride

[1,4'-Bipiperidine]-1'-carboxylic acid; CPT-11; (*S*)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester
$C_{33}H_{38}N_4O_6 \cdot HCl$ FW 623.14 [100286-90-6]
Antitumor agent. DNA topoisomerase inhibitor.
Ref: 1. Saijo, N, Preclinical and clinical trials of topoisomerase inhibitors. *Ann. N. Y. Acad. Sci.* **922**, 92 (2000)
2. Khayat, D., et al., The role of irinotecan and oxaliplatin in the treatment of advanced colorectal cancer. *Oncology* **15**, 415 (2001)
R: 22 RTECS # DW1061000 2-8°C

I1406-50MG	50 mg
I1406-250MG	250 mg

Levofloxacin

(–)-Ofloxacin
$C_{18}H_{20}FN_3O_4$ FW 361.37 [100986-85-4] BRN 7327015
***BioChemika*, ≥98.0% (HPLC)**
Antibiotic against bacterial respiratory tract infections[1,2]
Lit. cited: 1. G.G. Zhanel et al., *Drugs* **62**, 13 (2002)
2. M. Hurst et al., *Drugs* **62**, 2127 (2002)
R: 22-42/43-68 S: 26-36/37/39 RTECS # UU8815550

28266-10MG-F	10 mg
28266-1G-F	1 g
28266-10G-F	10 g

Inhibition of Nucleic Acid Synthesis

Norfloxacin

1-Ethyl-6-fluoro-1,4-dihydro-4-oxo-7-piperazino-3-quinolinecarboxylic acid
$C_{16}H_{18}FN_3O_3$ FW 319.33 [70458-96-7] EC No. 274 614 4
Norfloxacin blocks DNA replication by interfering with an ATP-induced structural transition of DNA complexed with DNA gyrase (topoisomerase).
Mode of action: Inhibits bacterial DNA replication
Antimicrobial spectrum: Gram-negative bacteria; less effective against Gram-positive bacteria
EC No. 274-614-4 RTECS # VB2005000 2-8°C

N9890-1G	1 g
N9890-5G	5 g
N9890-25G	25 g

Rifampicin

3-(4-Methylpiperazinyliminomethyl)rifamycin SV; Rifampin; Rifamycin AMP
$C_{43}H_{58}N_4O_{12}$ FW 822.94 [13292-46-1] EC No. 2363120 BRN 5723476
~95% (HPLC)
Mode of Action: Inhibits initiation of RNA synthesis by binding to β-subunit of RNA polymerase.

solubility
DMSO ..... 100 mg/mL
H_2O ..... 2.5 mg/mL at 25 °C, pH 7.3
H_2O ..... 1.3 mg/mL, pH 4.3

Ref: 1. Wehrli, W., Rifampin: mechanisms of action and resistance. *Rev. Infect. Dis.* **5**, S407-S411 (1983)
2. Mustaev, A., Topology of the RNA polymerase active center probed by chimeric rifampicin-nucleotide compounds. *Proc. Natl. Acad. Sci. USA* **91**, 12036 (1994)
3. Wegrzyn, A., et al., Differential inhibition of transcription from sigma70- and sigma32-dependent promoters by rifampicin. *FEBS Lett.* **440**, 172-174 (1998)
4. Pfannschmidt, T., et al., The A and B forms of plastid DNA-dependent RNA polymerase from mustard (*Sinapis alba L.*) transcribe the same genes in a different developmental context. *Mol. Gen. Genet.* **257**, 35-44 (1997)
5. Sodeik, B., et al., Assembly of vaccinia virus: effects of rifampin on the intracellular distribution of viral protein p65. *J. Virol.* **68**, 1103-1114 (1994)
6. Tomiyama, T., et al., Rifampicin prevents the aggregation and neurotoxicity of amyloid beta protein *in vitro*. *Biochem. Biophys. Res. Commun.* **204**, 76-83 (1994)

R: 22-36/37/38 S: 26-36 EC No. 236-312-0 RTECS # VJ7000000 -20°C

R3501-250MG	250 mg
R3501-1G	1 g
R3501-5G	5 g
R3501-25G	25 g

Inhibition of Protein Synthesis

Protein synthesis is a complex, multi-step process involving many enzymes as well as conformational alignment. However, the majority of antibiotics that block bacterial protein synthesis interfere with the processes at the 30S subunit or 50S subunit of the 70S bacterial ribosome. The aminoacyl-tRNA synthetases that activate each amino acid required for peptide synthesis are not antibiotic targets. Instead, the primary steps in the process that are attacked are (1) the formation of the 30S initiation complex (made up of mRNA, the 30S ribosomal subunit, and formyl-methionyl-transfer RNA), (2) the formation of the 70S ribosome by the 30S initiation complex and the 50S ribosome, and (3) the elongation process of assembling amino acids into a polypeptide.

Tetracyclines, including **doxycycline**, prevent the binding of aminoacyl-tRNA by blocking the A (aminoacyl) site of the 30S ribosome. They are capable of inhibiting protein synthesis in both 70S and 80S (eukaryotic) ribosomes, but they preferentially bind to bacterial ribosomes due to structural differences in RNA subunits. Additionally, tetracyclines are effective against bacteria by exploiting the bacterial transport system and increasing the concentration of the antibiotic within the cell to be significantly higher than the environmental concentration.

Aminoglycoside antibiotics have an affinity for the 30S ribosome subunit. **Streptomycin**, one of the most commonly used aminoglycosides, interferes with the creation of the 30S initiation complex. **Kanamycin** and **tobramycin** also bind to the 30S ribosome and block the formation of the larger 70S initiation complex.

Erythromycin, a macrolide, binds to the 23S rRNA component of the 50S ribosome and interferes with the assembly of 50S subunits. Erythromycin, roxithromycin, and clarithromycin all prevent elongation at the transpeptidation step of synthesis by blocking the 50S polypeptide export tunnel. Elongation is prematurely terminated after a small peptide has been formed but cannot move past the macrolide roadblock.

Peptidyl transferase is a key enzyme involved in translocation, the final step in the peptide elongation cycle. **Lincomycin** and clindamycin are specific inhibitors of peptidyl transferase, while macrolides do not directly inhibit the enzyme. **Puromycin** does not inhibit the enzymatic process, but instead competes by acting as an analog of the 3'-terminal end of aminoacyl-tRNA, disrupting synthesis and causing premature chain termination.

Hygromycin B is an aminoglycoside that specifically binds to a single site within the 30S subunit in a region that contains the A, P, and E sites of tRNA. It has been theorized that this binding distorts the ribosomal A site and may be the cause of the ability of hygromycin to induce misreading of aminoacyl-tRNAs as well as prevent the translocation of peptide elongation.

Doxycycline hyclate

Doxycycline hydrochloride hemiethanolate hemihydrate
$C_{22}H_{24}N_2O_8 \cdot HCl \cdot 1/2(H_2O) \cdot 1/2(C_2H_6O)$ FW 512.94 [24390-14-5]
EC No. 2341987
≥98% (TLC)
Broad spectrum antibiotic. Derivative of oxytetracycline. Inhibitor of MMP *in vivo*.
R: 22-36/37/38 S: 26 EC 234-198-7 RTECS # QI8925000 2-8°C

D9891-1G	1 g
D9891-5G	5 g
D9891-10G	10 g
D9891-25G	25 g
D9891-100G	100 g

Erythromycin

$C_{37}H_{67}NO_{13}$ FW 733.93 [114-07-8] EC No. 2040401 BRN 75279
Potency: ≥850 μg per mg
Mode of Action: Inhibits elongation at transpeptidation step.
Antimicrobial spectrum: Gram-negative and Gram-positive bacteria.

Macrolide antibiotic.
EC No. 204-040-1 RTECS # KF4375000

E6376-25G	25 g
E6376-100G	100 g

Hygromycin B

$C_{20}H_{37}N_3O_{13}$ FW 527.52 [31282-04-9] EC No. 2505455
from *Streptomyces hygroscopicus*
Mode of Action: Blocks polypeptide synthesis and inhibits elongation. For use in the selection and maintenance of prokaryotic and eukaryotic cells.
Purified by ion-exchange chromatography
R: 26/27/28-41-42/43 S: 22-26-28-36/37/39-45 EC No. 250-545-5 Lachrymator RTECS # WK2130000 2-8°C

H7772-50MG	50 mg
H7772-100MG	100 mg
H7772-250MG	250 mg
H7772-1G	1 g

Kanamycin disulfate salt

Kanamycin A; Kanamycin acid sulfate
[64013-70-3]
from *Streptomyces kanamyceticus,* Potency: ~650 μg per mg
Mode of Action: Binds to 70S ribosomal subunit; inhibits translocation; elicits miscoding.
Antimicrobial spectrum: Gram-negative and Gram-positive bacteria, and mycoplasma.
Kanamycin B ..... <5%
R: 61 S: 53-26-45

K1876-1G	1 g
K1876-5G	5 g
K1876-25G	25 g

Lincomycin hydrochloride

Lincocin hydrochloride; Methyl 6,8-dideoxy-6-(1-methyl-4-propyl-2-pyrrolidinecarboxamido)-1-thio-D-*erythro*-α-D-galactooctopyranoside hydrochloride
$C_{18}H_{34}N_2O_6S \cdot HCl$ FW 443.00 [859-18-7] EC No. 2127267
BRN 4171650
≥90% (TLC), Potency: 800-900 units per mg
Lincomycin is a lincosamide antibiotic that forms cross-links within the peptidyl transferase loop region of the 23S rRNA.[1]
Mode of action: Inhibits bacterial protein synthesis
Antimicrobial spectrum: Gram-positive bacteria
Lit. cited: 1. Kirillov, S. V., et al., Peptidyl transferase antibiotics perturb the relative positioning of the 3′-terminal adenosine of P/P′-site-bound tRNA and 23S rRNA in the ribosome *RNA* **5**, 1003-1013 (1999)
Ref: 2. Champney, W.S. and Tober, C.L., Specific inhibition of 50S ribosomal subunit formation in *Staphylococcus aureus* cells by 16-membered macrolide, lincosamide, and streptogramin B antibiotics *Curr. Microbiol.* **41**, 126-135 (2000)
R: 36/37/38 S: 26 EC No. 212-726-7 RTECS # RH6315000 2-8°C

L6004-1MU	1,000,000 units
L6004-5MU	5,000,000 units
L6004-25MU	25,000,000 units

Puromycin dihydrochloride

3′-[α-Amino-*p*-methoxyhydrocinnamamido]-3′-deoxy-N,N-dimethyladenosine dihydrochloride
$C_{22}H_{29}N_7O_5 \cdot 2HCl$ FW 544.43 [58-58-2] EC No. 2003878
BRN 3853613
from *Streptomyces alboniger,* ≥98% (TLC)
Nucleoside antibiotic. Protein synthesis inhibitor that causes premature chain termination by acting as an analog of the 3′-terminal end of aminoacyl-tRNA. Prevents growth of bacteria, protozoa, algae, and mammalian cells. Acts very quickly and can kill 99% of cells within 2 days. The resistance gene (puromycin acetyltransferase) gives very effective protection.
Recommended for use as a selection agent at a range of 10-100 μg/ml.
Ref: 1. de la Luna, S., Ortin, J., *pac* gene as efficient dominant marker and reporter gene in mammalian cells. *Meth. Enzymol.* **216**, 376 (1992)
2. Nathans, D., Gottlieb, D., Shaw, P.D., *Antibiotics* , Springer-Verlag (New York, NY: 1967), **1**, 259
R: 22 EC No. 200-387-8 RTECS # AU7355000 -20°C

P7255-25MG	25 mg
P7255-100MG	100 mg
P7255-250MG	250 mg
P7255-500MG	500 mg
P7255-1G	1 g

Streptomycin sulfate salt

$2C_{21}H_{39}N_7O_{12} \cdot 3H_2SO_4$ FW 1457.38 [3810-74-0] EC No. 2232860
BRN 3894995
Mode of Action: Inhibits prokaryote protein synthesis. Binds to S12 protein of 30S ribosomal subunit, preventing the transition from initiation complex to chain-elongating ribosome, causing miscoding or inhibiting initiation.
Mode of Resistance: Mutation in *rps*L (gene for S12 ribosomal protein) prevents binding of streptomycin to ribosome.
Antimicrobial spectrum: Gram-negative and Gram-positive bacteria.
R: 22 EC No. 223-286-0 RTECS # WK4990000 2-8°C

S6501-5G	5 g
S6501-25G	25 g
S6501-50G	50 g
S6501-100G	100 g
S6501-1KG	1 kg

Tobramycin sulfate salt

$C_{18}H_{37}N_5O_9 \cdot xH_2SO_4$ FW 467.51 (FB)
Spectrum of Activity: Gram negative bacteria. Not effective against *Enterococci*.
Mode of Action: Irreversible inhibition of bacterial protein synthesis.
R: 61-20/21/22 S: 53-22-36/37/39-45 2-8°C

T1783-100MG	100 mg
T1783-500MG	500 mg

Additional Modes of Antibiotic Action

Additional Modes of Antibiotic Action

A few antibiotics use less common mechanisms to attack bacteria. **Polymyxin B** and **colistin (polymyxin E)** disrupt the cell membrane integrity of Gram-negative bacteria by binding to membrane phospholipids. Eukaryotic cell membranes have phospholipids similar to Gram-negative bacteria, so the polymyxins are most often used clinically as topical antibiotics.

In contrast, the ionophore antibiotics such as **monensin** and **valinomycin** tend to be more active against Gram-positive bacteria, which lack the outer cell membranes. Monensin is an ionophore that forms monovalent ion channels in the cell wall of Gram-positive bacteria and allows the free movement of K^+ and Na^+ ions along their concentration gradients. Valinomycin is a selective K^+ ionophore that triggers mitochondrial transition by facilitating the transport of K^+ across the mitochondrial membrane. By altering the intracellular cationic environment of the cell, these agents uncouple mitochondrial oxidative metabolism and inhibit cell growth.

Colistin sulfate salt

Polymyxin E
[1264-72-8]
activity: ≥15,000 units/mg
Mode of Action: Binds to lipids on the cell cytoplasmic membrane of Gram-negative bacteria and disrupts the cell wall integrity.
Antimicrobial spectrum: Gram-negative bacteria.
Ref: 1. David, H.L., and Rastogi, N., Antibacterial action of colistin (polymyxin E) against *Mycobacterium aurum*. *Antimicrob. Agents Chemother.* **27**, 701-707 (1985)
2. Evans, M.E., et al., Polymyxin B sulfate and colistin: old antibiotics for emerging multiresistant Gram-negative bacteria. *Ann. Pharmacother.* **33**, 960-967 (1999)
R: 25 S: 45 EC No. 215-034-3 RTECS # TR1500000 2-8°C

C4461-100MG	100 mg
C4461-1G	1 g

Monensin sodium salt

Monensin A sodium salt
$C_{36}H_{61}NaO_{11}$ FW 692.85 [22373-78-0] EC No. 2449417 BRN 4122200
90-95% (TLC)
Na^+ ionophore; blocks glycoprotein secretion; may induce catecholamine secretion from chromaffin cells.
Ref: 1. Callaway, T.R., et al., Selection of a highly monensin-resistant *Prevotella bryantii* subpopulation with altered outer membrane characteristics. *Appl. Environ. Microbiol.* **65**, 4753-4759 (1999)
2. Wang, X.D., et al., Phospholipase C activation by Na^+/Ca^{2+} exchange is essential for monensin-induced Ca^{2+} influx and arachidonic acid release in FRTL-5 thyroid cells. *J. Investig. Med.* **47**, 388-396 (1999)
3. Nebbia, C., et al., Oxidative metabolism of monensin in rat liver microsomes and interactions with tiamulin and other chemotherapeutic agents: evidence for the involvement of cytochrome P-450 3A subfamily. *Drug Metab. Dispos.* **27**, 1039-1044 (1999)
R: 25 S: 36/37/39-45 EC No. 244-941-7 RTECS # JH2830000 2-8°C

M5273-500MG	500 mg
M5273-1G	1 g
M5273-5G	5 g

Polymyxin B sulfate salt

$C_{55}H_{96}N_{16}O_{13} \cdot 2H_2SO_4$ FW 1385.61 [1405-20-5] EC No. 2157747
activity: ≥6,000 USP units/mg
Antibiotic with bactericidal action on *E. coli*.[1,2] Binds to the lipid A portion of bacterial lipopolysaccharides.[3] Induces pore formation in the membranes of cortex cells from excised sorghum roots.[4]
Mode of Action: Binds to and interferes with the permeability of the cytoplasmic membrane.
Antimicrobial spectrum: Gram-negative bacteria.
Mixture of Polymyxin B_1 and B_2 sulfate.
Lit. cited: 1. Cornu, J., *Ann. Microbiol.* **131B**, 121 (1980)
2. Storm, D.R., et al., *Annu. Rev. Biochem.* **46**, 723 (1977)
3. Morrison, D.C. and Jacobs, D.M., *Immunochemistry* **13**, 813 (1976)
4. Lerner, H.R., et al., *Physiol. Plant.* **57**, 90 (1983)
R: 22 S: 22-24/25 EC No. 215-774-7 RTECS # TR1150000 2-8°C

P1004-1MU	1,000,000 units
P1004-5MU	5,000,000 units
P1004-10MU	10,000,000 units
P1004-25MU	25,000,000 units
P1004-50MU	50,000,000 units

Valinomycin

Cyclo(L-Val-D-Hylva-D-Val-L-Lac-)$_3$: Hylva = α-Hydroxyisovaleric acid, Lac = Lactic acid
$C_{54}H_{90}N_6O_{18}$ FW 1111.32 [2001-95-8] EC No. 2178966 BRN 78657
≥90% (HPLC)
K^+-selective ionophoric cyclodepsipeptide; potassium ionophore which uncouples oxidative phosphorylation, induces apoptosis in murine thymocytes, inhibits NGF-induced neuronal differentiation and antagonizes ET-induced vasoconstriction.
solubility
H_2O ..... insoluble
DMSO ..... ≥10 mg/mL
Ref: 1. Inai, Y, et al., Valinomycin induces apoptosis of ascites hepatoma cells (AH-130) in relation to mitochondrial membrane potential. *Cell Struct. Funct.* **22**, 555-563 (1997)
2. Furlong, I.J., et al., Induction of apoptosis by valinomycin: mitochondrial permeability transition causes intracellular acidification. *Cell Death Differ.* **5**, 214-221 (1998)
3. Andersson, M.A., et al., The mitochondrial toxin produced by *Streptomyces griseus* strains isolated from an indoor environment is valinomycin. *Appl. Environ. Microbiol.* **64**, 4767-4773 (1998)
R: 27/28 S: 28-36/37-45 EC No. 217-896-6 RTECS # YV9468000 2-8°C

V0627-10MG	10 mg
V0627-25MG	25 mg
V0627-100MG	100 mg
V0627-500MG	500 mg

Antibiotic Ready Made Solutions

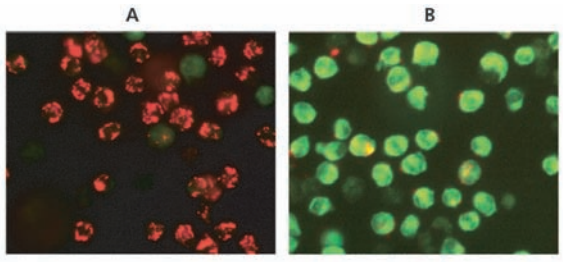
Sigma-Aldrich's Antibiotic Ready Made Solutions arrive at your laboratory as sterile-filtered, ready to use formulations. Ready Made antibiotic solutions minimize your exposure to potentially harmful powders, reducing your risk as well as saving your time. All Ready Made Solutions are 0.2 µm filtered for extended shelf life and prevention of bacterial contamination. As with all Sigma-Aldrich products, strict quality control measures apply to each Ready Made Solution.

Apoptosis Induced by Valinomycin Ready Made Solution

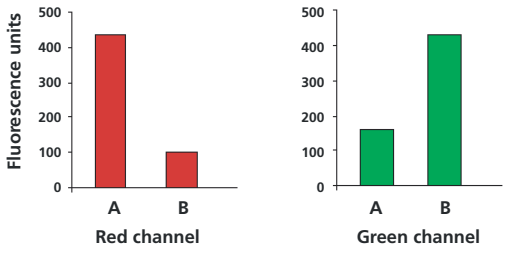
The ionophoric functionality of valinomycin enables its use as a tool for apoptosis induction by disrupting the mitochondrial membrane potential. Valinomycin triggers rapid loss of the mitochondrial membrane potential, causing cytoplasmic acidification and leading to protease activation, DNA fragmentation, and cell death.[1,2]

Valinomycin Ready Made Solution (V3639) has been used to induce apoptosis in U937 cells and Jurkat cells, as detected using the fluorescent JC-1 dye contained in the Mitochondria Staining Kit (CS0390).

In normal cells, due to the electrochemical potential gradient, the JC-1 dye concentrates in the mitochondrial matrix, where it forms red fluorescent aggregates. Any event that dissipates the mitochondrial membrane potential (e.g., apoptosis) prevents the accumulation of the JC-1 dye in the mitochondria. The dye is dispersed throughout the entire cell, resulting in a shift from red fluorescence (J-aggregates) to green fluorescence (JC-1 monomers).



JC-1 staining of control versus Valinomycin treated cells
Control U937 cells (A) and U937 cells treated with Valinomycin Ready Made Solution (V3639, 100 nM final concentration) (B) were stained with JC-1 dye using the Mitochondria Staining Kit (CS0390) and visualized under an Olympus IX81 fluorescence microscope. Normal cells show red, granular mitochondrial staining, whereas valinomycin treated cells show diffuse, green cytoplasmic staining.



JC-1 fluorescence shift in Valinomycin treated versus untreated Jurkat cells
Jurkat cells were stained with JC-1 using the Mitochondria Staining Kit (CS0390). Valinomycin Ready Made Solution was added to a final concentration of 100 nM to Sample B during staining while Control A remained untreated. The shifts in the red (530 nm excitation and 590 nm emission wavelength) and the green channels (490 nm excitation and 530 nm emission wavelength) were measured using a Perkin Elmer LS50B fluorimeter. Mitochondrial potential dissipation induced by Valinomycin Ready Made Solution caused a decrease in the red fluorescence concurrently with an increase in the green fluorescence.

1. Inai, Y., *et al.*, Valinomycin induces apoptosis of ascites hepatoma cells (AH-130) in relation to mitochondrial membrane potential. *Cell Struct. Funct.*, **22**, 555-563 (1997).
2. Furlong, I. J., *et al.*, Induction of apoptosis by valinomycin: mitochondrial permeability transition causes intracellular acidification. *Cell Death Differ.*, **5**, 214-221 (1998).

Recommended for use as selection agents

Ampicillin

Ready Made Solution, 100 mg/mL, 0.2 µm filtered

A β-lactam antibiotic with an amino group side chain attached to the penicillin structure. Penicillin derivative that inhibits bacterial cell-wall synthesis (peptidoglycan cross-linking) by inactivating transpeptidases on the inner surface of the bacterial cell membrane. Bactericidal only to growing *Escherichia coli.* Mode of resistance: Cleavage of β-lactam ring of ampicillin by β-lactamase. Antimicrobial spectrum: Gram-negative and Gram-positive bacteria.

Ampicillin in a convenient ready-to-use solution useful in selecting for bacteria cells with specific resistance.

R: 36/37/38-42/43 S: 26-36/37-45 ◆ -20°C DRY ICE

A5354-10ML	10 mL

Carbenicillin

Ready Made Solution, 100 mg/mL in ethanol/water, 0.2 µm filtered

Carbenicillin is found to be less sensitive then ampicillin to the destructive activity of β-lactamase. In addition it has a superior stability at low pH. Experiments have shown that the use of carbenicillin in place of ampicillin helps prevent overgrowth of satellite colonies. Carbenicillin should be used at a concentration of 50 to 100 µg/ml.

Ref: 1. Wright, A.J., *Mayo Clin. Proc.* **74**, 290-307 (1999)
2. Asubusel, F.M., et al., *Current Protocols in Molecular Biology* , John Wiley & Sons, **1**, 8.9
3. Rolinson, G.N., *J. Antimicrob. Chemother.* **41**, 589-603 (1998)

R: 10-42/43 S: 36/37 Fp: 40 °C (104 °F) -20°C WET ICE

C1613-1ML	1 mL

Antibiotic Ready Made Solutions

Recommended for use as selection agents

Puromycin

Ready Made Solution, from *Streptomyces alboniger*, 10 mg/mL in H_2O, 0.2 µm filtered, ≥98% (HPLC)

Puromycin inhibits the growth of a wide range of eukaryotic and prokaryotic cells by interfering with protein synthesis. It allows the selection of cells expressing the *pac* gene.

Tested on HeLa cells for cell growth arrest and selection of cells after transfection of the *pac* resistance gene.

Cell culture tested

Ref: 1. Tabuchi, I., *Biochem. Biophys. Res. Commun.* **23**, 2-5 (2003)
2. Eyckerman, S., et al., *Nat. Cell Biol.* **3**, 1114-1116 (2001)

R: 22 S: 36 EC No. 200-387-8 RTECS # AU7355000 -20°C WET ICE

P9620-10ML	10 mL

Spectinomycin

Ready Made Solution, 100 mg/mL in DMSO/H_2O (1:1), 0.2 µm filtered

Broad spectrum antibiotic produced by the soil bacterium *Streptomyces spectabilis*. Spectinomycin inhibits protein synthesis (elongation) by binding to the bacterial 30S ribosomal subunit and interfering with peptidyl tRNA translocation. Resistance to spectinomycin is conferred by aminoglycoside-3'-adenyltransferase gene (*aadA*).

Spectinomycin is used as a selection marker in plant related transformation systems. Spectinomycin is also used for amplification of low copy number plasmid carrying replicons as Col E1, pMB1 (pBR322 and its derivatives), and p15A/rep (pACYC and its derivatives). The replication of these plasmids relies on long-lived enzymes supplied by the host. Addition of spectinomycin to the plasmid containing cells inhibits replication of the host, while the plasmids continue to replicate for 10-15 hours. The copy number of the plasmid can increase 100-fold, from 20-30 copies to 3000 copies as in the case of ColE1.

Inhibits bacteria (*E.coli* DH5α) growth at a concentration of 100 µg/ml.

Ref: 1. Holloway, W.J., *Med. Clin. North Amer.* **66**, 169-73 (1982)
2. Carter, A.P., et al., *Nature* **407**, 340-348 (2000)
3. Chang, C.Y, et al., *J. Antimicrob. Chemother.* **46**, 87-9 (2000)
4. Khan, M.S. and Maliga, P., *Nat. Biotechnol.* **17**, 855-6 (1999)
5. Sambrook, J., et al., *Molecular Cloning: A Laboratory Manual* 2ndth ed., Cold Spring Harbor Laboratory Press (1989), 1.3-1.5
6. Ausubel, F.M., et al. , *Current Protocols in Molecular Biology* , Wiley (1987), 1.5.1-1.5.4
7. Chang, A.C.Y. and Cohen, S.N., *J. Bacteriol.* **134**, 1141-56 (1978)

Fp: 94 °C (201 °F) Hygroscopic -20°C WET ICE

S0692-1ML	1 mL

Recommended for use in antineoplastic research studies

Also useful as antibacterial, antifungal, or antimycobacterial agents

Cycloheximide solution

CHX

Ready Made Solutions, microbial, 100 mg/mL in DMSO, 0.2 µm filtered

Cycloheximide (CHX) is an antibiotic produced by *S. griseus*. Its main biological activity is translation inhibition in eukaryotes resulting in cell growth arrest and cell death. CHX is widely used for selection of CHX-resistant strains of yeast and fungi, controlled inhibition of protein synthesis for detection of short-lived proteins and super-induction of protein expression, and apoptosis induction or facilitation of apoptosis induction by death receptors.

Tested for cell growth arrest, selection of cycloheximide resistant yeast, apoptosis induction, and facilitation of apoptosis induction by FasL.

Ref: 1. Kominek, L.A., *Antimicrob. Agents Chemother.* **7**, 856 (1975)
2. Smith, A.D., et al., *Dictionary of Microbiology and Molecular Biology* (1997)
3. Lennette, E.H., et al., *Manual of Clinical Microbiology* 4th ed., ASM (Washington D.C.: 1985), 500
4. Lin, W.W., and Hsu, Y.W., *Cell. Signal.* **12**, 457 (2000)
5. Mizel, S.B., and Mizel, D., *J. Immunol.* **126**, 834 (1981)
6. Ma, Q., et al., *J. Biol. Chem.* **275**, 12676 (2000)
7. Clemens, M.J., et al., *Oncogene* **17**, 2921 (1998)
8. Fulda, S., *Cancer Res.* **60**, 3947 (2000)

R: 61-28-52/53-68 S: 53-45 Fp: 87 °C (189 °F) Hygroscopic 2-8°C

C4859-1ML	1 mL

Ionomycin calcium salt

Ready Made Solution, from *Streptomyces conglobatus*, 1 mM in DMSO, 0.2 µm filtered, ≥98% (HPLC)

Ca^{2+} ionophore that is more effective than A23187 as a mobile ion carrier for Ca^{2+}; non-fluorescent; used to study Ca^{2+} transport across biological membranes; induces apoptotic degeneration of embryonic cortical neurons.

Ref: 1. Toeplitz, B.K., et al., *J. Am. Chem. Soc.* **101**, 3344 (1979)

Fp: 87 °C (189 °F) Hygroscopic -20°C WET ICE

I3909-1ML	1 mL

Staurosporine

Antibiotic AM-2282

Ready Made Solution, from *Streptomyces* sp., 1 mM in DMSO (100 µg/214 µL), 0.2 µm filtered, ≥98% (HPLC)

Potent inhibitor of phospholipid/calcium-dependent protein kinase. Inhibits the upregulation of VEGF expression in tumor cells.

Cell culture tested

Ref: 1. Windham. T.C., et al., *Oncogene* **21**, 7797-807 (2002)
2. Nishi, K., et al., *Exp. Cell Res.* **280**, 233-43 (2002)

Fp: 87 °C (189 °F) Hygroscopic -20°C WET ICE

S6942-200UL	200 µL

Valinomycin

Ready Made Solution, ~1 mg/mL in DMSO, 0.2 µm filtered, ≥90% (HPLC)

K^+-selective ionophoric cyclodepsipeptide; potassium ionophore which uncouples oxidative phosphorylation, induces apoptosis in murine thymocytes, inhibits NGF-induced neuronal differentiation and antagonizes ET-induced vasoconstriction.

Ref: 1. Inai, Y, et al., Valinomycin induces apoptosis of ascites hepatoma cells (AH-130) in relation to mitochondrial membrane potential. *Cell Struct. Funct.* **22**, 555-563 (1997)
2. Furlong, I.J., et al., Induction of apoptosis by valinomycin: mitochondrial permeability transition causes intracellular acidification. *Cell Death Differ.* **5**, 214-221 (1998)
3. Andersson, M.A., et al., The mitochondrial toxin produced by *Streptomyces griseus* strains isolated from an indoor environment is valinomycin. *Appl. Environ. Microbiol.* **64**, 4767-4773 (1998)

R: 21/22 S: 36 Fp: 87 °C (189 °F) Hygroscopic 2-8°C WET ICE

V3639-5ML	5 mL

Antibiotics for Plant Tissue Culture

One of the primary applications for antibiotics in research is to support selective cell growth by preventing the growth of undesired cells. To that end, antibiotics are used in plant tissue culture media to eliminate contamination. The following antibiotics are tested specifically for use in plant tissue culture.

For over 20 years, Sigma-Aldrich has consistently supplied a diverse range of products for plant research. From genomics to proteomics, tissue culture protocols, and lab equipment, Sigma-Aldrich delivers technical resources and innovative tools for the future of plant research. For a complete listing of our genomic, proteomic, and immunochemistry products, please visit **sigma-aldrich.com/plant.**
Image courtesy of David L. Carlton, Texas A&M University.

Antibiotics Reference Guide for Plant Tissue Culture

Product	Cat. No.	Mol. Wt.	Gram (+) bacteria	Gram (-) bacteria	Myco-bacteria	Myco-plasma	Toxicity to microbes (µg/mL)	Toxicity to plant tissue (µg/mL)	Working conc. (µg/mL) and applications[1]	Product Solubility	Solution Storage
Carbenicillin	**C3416**	422.4	X	XX			500	>1000	up to 500 (CC,PR,EC)	Water	-0 °C 2–8 °C 3 days
Cefotaxime	**C7039**	477.4	X	XX			90	>100	up to 500 (CC,PR,EC)	Water	-0 °C 2–8 °C 22 days
Chloramphenicol	**C1919**	323.1	XX	XX	X	X	128	>1	10–35 (TS)	EtOH	2–8 °C 30 days
G418 disulfate salt	**G1279**	692.7							10–500	Water	-20 °C 6 mo.
Gentamicin sulfate	**G6896**		X	XX		XX	50	>50	up to 250 (CC)	Water	2–8 °C 12 mo.
Hygromycin B	**H9773**	527.5							100–200	Water	2–8 °C 6 mo.
Kanamycin sulfate	**K4378**	582.6	XX	XX		XX	100	>2	16 (SSC); up to 40 (CC,PR,EC)	Water	2–8 °C 12 mo.
Paromycin sulfate	**P8692**	615.6	XX	X						Water	2–8 °C 21 days
Penicillin G, potassium salt	**P8306**	372.5	XX	X			1005		up to 100	Water	2–8 °C 4 days
Penicillin G, sodium salt	**P8431**	356.4	XX	X			1005		up to 100	Water	2–8 °C 4 days
Rifampicin	**R7382**	823.0	XX	XX	XX		15	>25	50 (TS); up to 25 (PC,TEC)	DMSO	2–8 °C 1 day
Streptomycin sulfate	**S0774**	1457.4	X	XX	X		100	>16		Water	2–8 °C 30 days
Vancomycin	**V1130**	1485.7	XX				5	>100	up to 10 (PC); up to 40 (CC,EC,STM)	Water	2–8 °C 7 days

XX = Effective against most species
X = Effective against certain species
[1]**Application key:** CC = callus culture; PR = plant regeneration; EC = cotyledon, hypocotyl, or leaf disc culture; TS = transformant selection; SSC = stem section culture; PC = protoplast culture; TEC = tuber explant culture; STM = shoot tip micropropagation

Preparation of Selected Antibiotics

Carbenicillin

Carbenicillin is a white to off-white hygroscopic powder that is soluble in either water or alcohol. Carbenicillin is most effective against Gram-negative bacteria, but may also have some effect against Gram-positive bacteria. Aqueous solutions of carbenicillin are reported to be stable for up to 24 hours at room temperature, and for up to 72 hours when stored at 2-8 °C.

Carbenicillin disodium salt

α-Carboxybenzylpenicillin disodium salt

$C_{17}H_{16}N_2Na_2O_6S$ FW 422.36 [4800-94-6] EC No. 2253608

BRN 5722128

Plant cell culture tested

Carboxypenicillin antibiotic that inhibits bacterial cell-wall synthesis (peptidoglycan cross-linking) by inactivating transpeptidases on the inner surface of the bacterial cell membrane. Analog to ampicillin. Antimicrobial spectrum: Gram-positive and Gram-negative bacteria, *Pseudomonas*.

Recommended for antibacterial use in cell culture media at 100 µg/ml.

solubility

H_2O ..... 50 mg/mL

Ref: 1. Mandell, G., Antibacterial agents: Penicillins, cephalosporins, and other β-lactam antibiotics. *Goodman and Gilman's The Pharmacological Basis of Therapeutics* 9th ed., McGraw-Hill (New York, NY: 1996), 1074

2. Raleigh, E.A. , *Escherichia coli*, plasmids and bacteriophages. *Short Protocols in Molecular Biology* 2nd ed., Greene Publishing Associates and John Wiley & Sons (New York, NY: 1992), 1

3. Perlman, D, Use of antibiotics in cell culture media. *Meth. Enzymol.* , Academic Press (New York, NY: 1979), **LVIII**, 112

R: 42/43 S: 22-36/37 EC No. 225-360-8 RTECS # ON9105000 2-8°C

C3416-250MG	250 mg
C3416-1G	1 g
C3416-5G	5 g
C3416-10G	10 g

Cefotaxime

Cefotaxime is a white to off-white powder that is freely soluble in water. Variations in color of the freshly prepared solutions do not necessarily indicate changes in potency. Store this product in an airtight container protected from light. Aqueous solutions of cefotaxime at a pH of 4.3-6.2 are stable for 14-21 days when stored at 2-8 °C. Cefotaxime is most effective against Gram-negative bacteria.

Cefotaxime sodium salt

Cefotaxim sodium salt

$C_{16}H_{16}N_5NaO_7S_2$ FW 477.45 [64485-93-4] EC No. 2649159

BRN 5711411

Plant cell culture tested, ~95%

Mode of Action: Inhibits bacterial cell wall synthesis.

Broad spectrum third generation cephalosporin antibiotic.

solubility

H_2O ..... soluble

R: 42/43 S: 22-36/37 EC No. 264-915-9 RTECS # XI0250000 2-8°C

C7039-100MG	100 mg
C7039-500MG	500 mg
C7039-1G	1 g
C7039-5G	5 g
C7039-10G	10 g

G418 disulfate salt

Although it is related to Gentamicin, G418 disulfate salt is not normally used as a standard antibiotic. Its most common application is in molecular biology as a selection agent. G418 is toxic to bacteria, yeast, protozoa, helminths, and mammalian cells. Resistance is conferred by one of two dominant genes of bacterial origin, which can be expressed in eukaryotic cells.

G418 disulfate salt is water soluble and can be stored at room temperature for as long as 1 year. Aqueous solutions should be stored frozen. The amount of G418 disulfate salt required for selection will vary with each cell type and growth cycle. Although cells that are multiplying will be affected sooner than those that are not, cells that are in log phase will still require 3 to 7 days for selection.

G 418 disulfate salt

Antibiotic G418

$C_{20}H_{40}N_4O_{10} \cdot 2H_2SO_4$ FW 692.71 [108321-42-2]

Plant cell culture tested, ~98% (TLC)

Mode of Action: Blocks polypeptide synthesis by inhibiting protein elongation. For use in the selection and maintenance of eukaryotic cells stably transfected with neomycin resistance genes.

Aminoglycoside antibiotic similar in structure to gentamicin, neomycin, and kanamycin.

S: 22-24/25 2-8°C

G1279-250MG	250 mg
G1279-1G	1 g
G1279-5G	5 g

Hygromycin B

Hygromycin B is an aminoglycoside antibiotic that is effective against prokaryotic and eukaryotic micro-organisms and cells. Similar to G418 disulfate salt, its most common application is in molecular biology as a selection agent. Insect and mammalian cells transformed with the *hph* gene, which encodes for hygromycin-B-phosphotransferase, are resistant to hygromycin B. The recommended concentration range for use as a selection agent is 10 - 400 µg/ml. Additional recommended concentrations are:

Prokaryotes - 100 µg/ml
Lower eukaryotes - 200 µg/ml
Higher eukaryotes - 150-400 µg/ml

Hygromycin B

$C_{20}H_{37}N_3O_{13}$ FW 527.52 [31282-04-9] EC No. 2505455

from *Streptomyces hygroscopicus,* Plant cell culture tested, ≥60% (HPAE)

Mode of Action: Blocks polypeptide synthesis and inhibits elongation. For use in the selection and maintenance of prokaryotic and eukaryotic cells.

Purified by ion-exchange chromatography

R: 26/27/28-41-42/43 S: 22-26-28-36/37/39-45 EC No. 250-545-5 Lachrymator RTECS # WK2130000 2-8°C

H9773-50MG	50 mg
H9773-100MG	100 mg
H9773-250MG	250 mg

Nystatin
Nystatin is an antifungal agent produced from *Streptomyces* sp. It exhibits fungicidal and fungistatic activity when prepared as an aqueous suspension. Nystatin is only slightly soluble in water and alcohol. Aseptic suspensions can be prepared by surface sterilizing the powder in a small amount of dimethyl sulfoxide (DMSO) (to wet the powder) and then suspending the powder in sterile water. This procedure should be performed under aseptic conditions with sterile equipment (glassware, etc.)
Nystatin preparations are heat labile. Aqueous suspensions should be stored below 0 °C and protected from light. Nystatin suspensions should have a pH of 6.5-8.0 and will decompose at a pH below 2.0 or above 9.0.

Nystatin

Fungicidin ; Mycostatin
[1400-61-9] EC No. 2157490
Plant cell culture tested
Mode of Action: Increases the permeability of the cell membrane of sensitive fungi by binding to sterols.
Antimicrobial spectrum: Yeasts and molds.
Minimum 5000 USP units/mg.
Ref: 1. Brezis, M., *Science* **224**, 66 (1984)
S: 22-24/25 EC No. 215-749-0 RTECS # RF5950000 -20°C

N9767-5MU	5,000,000 units
N9767-25MU	25,000,000 units

Additional Antibiotics for Plant Tissue Culture

Chloramphenicol

Chloromycetin; D-(–)-*threo*-2-Dichloroacetamido-1-(4-nitrophenyl)-1,3-propanediol
$C_{11}H_{12}Cl_2N_2O_5$ FW 323.13 [56-75-7] EC No. 2002874 BRN 2225532
Plant cell culture tested
Mode of Action: Inhibits translation on the 50S ribosomal subunit at the peptidyltransferase step (elongation inhibition). Bacteriostatic.
Mode of Resistance: Acetylation by chloramphenicol acetyltransferase (*cat* gene).
R: 45 S: 53-45 EC No. 200-287-4 Light sensitive RTECS # AB6825000

C1919-5G	5 g
C1919-25G	25 g
C1919-100G	100 g

Gentamicin sulfate salt

[1405-41-0]
Plant cell culture tested
Mode of action: Gentamicin causes codon misreading by binding to the 30S ribosomal subunit, blocking the translocation of peptidyl-tRNA from the acceptor site to the donor site.[1,2] The bactericidal effect of gentamicin on *Pseudomonas aeruginosa* is exerted by the binding of gentamicin to the outer membrane, where it displaces natural cations, destabilizes the membrane, and forms holes in the cell surface.[3]
Antimicrobial spectrum: Gram-negative bacteria, *Staphylococcus aureus* and other Gram-positive bacteria
Potency: ~600 µg gentamicin per mg
Lit. cited: 1. Korzybski, T., et al., *Antibiotics: origin, nature, and properties* , American Society for Microbiology (Washington, DC: 1977), 712-723
2. Lorian, V. (ed.), *Antibiotics in Laboratory Medicine* 2nd ed., Williams and Wilkins (Baltimore, MD: 1986), 694-696
3. Kadurugamuwa, J., et al., Surface action of gentamicin on *Pseudomonas aeruginosa J. Bacteriol.* **175**, 5798-5805 (1993)

R: 42/43 S: 22-36/37-45 EC No. 215-778-9 RTECS # LY2625000 2-8°C

G6896-1G	1 g
G6896-5G	5 g
G6896-10G	10 g

Kanamycin sulfate

Kanamycin A
$C_{18}H_{36}N_4O_{11} \cdot H_2O_4S$ FW 582.58 [25389-94-0]
from *Streptomyces kanamyceticus*, Plant cell culture tested
Mode of Action: Binds to 70S ribosomal subunit; inhibits translocation; elicits miscoding.
Antimicrobial spectrum: Gram-negative and Gram-positive bacteria, and mycoplasma.
Potency: ≥750 µg per mg
Kanamycin B ..... <5%
EC No. 246-933-9 RTECS # NZ3225030

K4378-5G	5 g
K4378-25G	25 g

Paromomycin sulfate salt

$C_{23}H_{45}N_5O_{14} \cdot H_2SO_4$ FW 713.71 [1263-89-4] EC No. 2150317
BRN 5715182
Plant cell culture tested
Antimicrobial spectrum: Gram-negative and Gram-positive bacteria, some protozoan species, and limited antihelminth.
Mode of Action: Inhibits initiation and elongation during protein synthesis.
R: 68/20/21/22 S: 36/37 EC No. 215-031-7 RTECS # WK2320000

P8692-5G	5 g
P8692-25G	25 g

▼ Penicillin G

Penicillin G potassium salt

Benzylpenicillin potassium salt
$C_{16}H_{17}KN_2O_4S$ FW 372.48 [113-98-4] EC No. 2040380 BRN 3832841
Plant cell culture tested, activity: ~1,600 units/mg
Mode of Action: Inhibits bacterial cell wall synthesis.
Antimicrobial spectrum: Gram-positive bacteria
R: 42/43 S: 36/37 EC No. 204-038-0 RTECS # XH9700000

P8306-100MU	100,000,000 units

Penicillin G sodium salt

Benzylpenicillin sodium salt
$C_{16}H_{17}N_2NaO_4S$ FW 356.37 [69-57-8] EC No. 2007102 BRN 3834217
Plant cell culture tested, activity: ~1,650 units/mg
Mode of Action: Inhibits bacterial cell wall synthesis.
Antimicrobial spectrum: Gram-positive bacteria.
Ref: 1. Martin, H.H. and Gmeiner, J., Modification of peptidoglycan structure by penicillin action in cell walls of *Proteus mirabilis*. *Eur. J. Biochem.* **95**, 487 (1979)
R: 42/43 S: 22-36/37-45 EC No. 200-710-2 RTECS # XH9800000

P8431-100MU	100,000,000 units

Penicillin G ▲

Additional Antibiotics for Plant Tissue Culture

Rifampicin

3-(4-Methylpiperazinyliminomethyl)rifamycin SV; Rifampin; Rifamycin AMP
$C_{43}H_{58}N_4O_{12}$ FW 822.94 [13292-46-1] EC No. 2363120 BRN 5723476
Plant cell culture tested, ~95% (HPLC)

Mode of Action: Inhibits initiation of RNA synthesis by binding to β-subunit of RNA polymerase.

Ref: 1. Wehrli, W., Rifampin: mechanisms of action and resistance. *Rev. Infect. Dis.* **5**, S407-S411 (1983)
2. Mustaev, A., Topology of the RNA polymerase active center probed by chimeric rifampicin-nucleotide compounds. *Proc. Natl. Acad. Sci. USA* **91**, 12036 (1994)
3. Wegrzyn, A., et al., Differential inhibition of transcription from sigma70- and sigma32-dependent promoters by rifampicin. *FEBS Lett.* **440**, 172-174 (1998)
4. Pfannschmidt, T., et al., The A and B forms of plastid DNA-dependent RNA polymerase from mustard (*Sinapis alba L.*) transcribe the same genes in a different developmental context. *Mol. Gen. Genet.* **257**, 35-44 (1997)
5. Sodeik, B., et al., Assembly of vaccinia virus: effects of rifampin on the intracellular distribution of viral protein p65. *J. Virol.* **68**, 1103-1114 (1994)

R: 22-36/37/38 S: 26-36 EC No. 236-312-0 RTECS # VJ7000000 -20°C

R7382-1G	1 g
R7382-5G	5 g

Streptomycin sulfate salt

$2C_{21}H_{39}N_7O_{12} \cdot 3H_2SO_4$ FW 1457.38 [3810-74-0] EC No. 2232860
BRN 3894995
Plant cell culture tested, ~95% (HPLC)

Mode of Action: Inhibits prokaryote protein synthesis. Binds to S12 protein of 30S ribosomal subunit, preventing the transition from initiation complex to chain-elongating ribosome, causing miscoding or inhibiting initiation.

Mode of Resistance: Mutation in *rps*L (gene for S12 ribosomal protein) prevents binding of streptomycin to ribosome.

Antimicrobial spectrum: Gram-negative and Gram-positive bacteria.

R: 22 EC No. 223-286-0 RTECS # WK4990000 2-8°C

S0774-25G	25 g
S0774-100G	100 kg

Vancomycin hydrochloride

$C_{66}H_{75}Cl_2N_9O_{24} \cdot HCl$ FW 1485.71 [1404-93-9] BRN 3704657
from *Streptomyces orientalis*, Plant cell culture tested

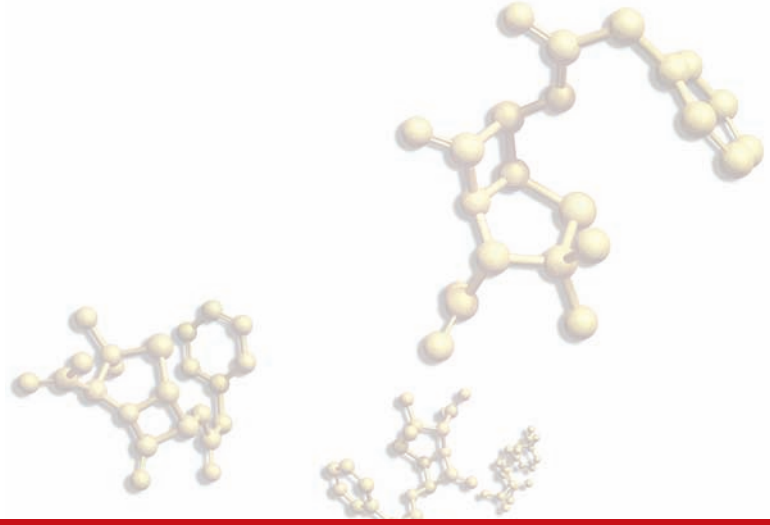
Glycopeptide antibiotic
Mode of action: interferes with cell wall synthesis
Antimicrobial spectrum: Gram-positive bacteria
potency: ~1,000 µg per mg

Studies on bond strength in vancomycin-peptide complexes;[1] Structure of vancomycin and its complex with acetyl-D-alanyl-D-alanine.[2]

Lit. cited: 1. Williamson, M.P., and Williams, D.H., *Eur. J. Biochem.* **138**, 345 (1984)
2. Sheldrick, et al., *Nature* **271**, 223 (1978)

R: 43 S: 36/37 RTECS # YW4380000 2-8°C

V1130-1G	1 g
V1130-5G	5 g



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Antibiotic use is widespread in livestock production to control infection and promote growth. Development of antibiotic-resistant microorganisms has been linked to overuse of antibiotics in livestock.[1,2,3] As consumers become more aware of the negative impact on human health due to bacterial antibiotic resistance, concern about the presence of residual antibiotics in the human food supply has increased.[4,5,6] The United Nations FAO/WHO Expert Committee on Food Additives (JECFA) has recommended maximum levels of veterinary drug residues entering the human food supply.

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References:

1. Animal antibiotic use has an early but important impact on the emergence of antibiotic resistance in human commensal bacteria. Smith D.L., et al., *Proc. Natl. Acad. Sci. USA* **99**, 6434–6439 (2002).
2. The food safety perspective of antibiotic resistance (Review). McDermott P.F., et al., *Anim. Biotechnol.* **13**, 71-84 (2002).
3. Antimicrobial resistance among Gram-negative foodborne bacterial pathogens associated with foods of animal origin. (Review) White, D.G., et al., *Foodborne Pathog. Dis.*, **1**,137-52 (2004).
4. United States Food and Drug Administration website "Antibiotic Resistance", http://www.fda.gov/oc/opacom/hottopics/anti_resist.html
5. European Commission RTD Info Magazine on European Research, "Fighting microbial resistance" No. 37, 2003 http://ec.europa.eu/research/rtdinfo/37/article_60_en.html
6. Japanese Regulatory Framework for the Control of Residues of Veterinary Drugs, Food and Agricultural Organization of the United Nations, http://www.fao.org/docrep/008/y5723e/y5723e0r.htm

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Amphotericin B trihydrate	46006-100MG
Ampicillin trihydrate	46061-250MG-R
Atrazine-desethyl-desisopropyl-2-hydroxy	45613-250MG
Bacitracin A	46084-250MG-R
Benzathine penicilline G tetrahydrate	46610-250MG-R
Cefalexin	33989-100MG-R
Chloramphenicol	46110-250MG-R
Chlortetracycline hydrochloride	46133-250MG-R
Cloxacillin sodium salt hydrate	46140-250MG-R
Demeclocyclin hydrochloride hemihydrate	46161-100MG
Dicloxacillin sodium salt hydrate	46182-100MG
Dimetridazole	46224-250MG-R
Doxycycline hyclate	33429-100MG-R
Enrofloxacin	33699-100MG-R
Fosfomycin sodiunm salt	34089-100MG
Furazolidone	46297-250MG
Gentamycin sulfate salt hydrate	46305-250MG
Griseofulvin	46309-250MG
Lincomycin hydrochloride monohydrate	46387-250MG-R
Monensin sodium salt	46468-100MG
Morantel tartrate hydrate	46473-250MG
Neomycin B trisulfate hydrate	33492-100MG-R
Nitrofurantoin	46502-250MG
Novobiocin sodium salt	46531-250MG
Ofloxacin	33703-100MG-R
Oxytetracycline hydrochloride	46598-250MG-R
Penicillin G potassium salt	46609-250MG

Product Name	Cat. No.
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Polymyxin B pentahemisulfate pentahydrate	46639-100MG
Praziquantel	46648-250MG
Rifamycin SV sodium salt hexahydrate	46721-100MG
Spectinomycin dihydrochloride pentahydrate	46738-250MG
Spiramycin	46745-100MG
Streptomycin sesquisulfate	46754-250MG
N^4-Succinylsulfathiazole monohydrate	46900-250MG-R
Sulfabenzamide	46762-250MG
Sulfacetamide	46770-250MG
Sulfachloropyridazine	46778-250MG
Sulfadiazine	35033-100MG
Sulfadimethoxine	46794-250MG
Sulfaguanidine monohydrate	46818-250MG
Sulfamerazine	46826-250MG
Sulfameter	46834-250MG
Sulfamethazine	46802-250MG
Sulfamethizole	46842-250MG-R
Sulfamethoxazole	46850-250MG-R
Sulfamethoxypyridazine	46858-250MG-R
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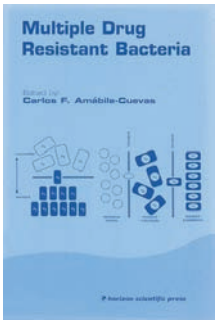
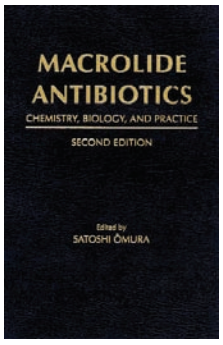
Z702986 Antibiotics: Actions, Origins, Resistance

This text offers a comprehensive account of the structural classes of antibiotics. While most of the attention is on natural products, synthetic chemicals with antibiotic activity are also discussed. The book contains a section that examines how antibiotics block specific proteins acting in these essential bacterial processes and how the molecular structure of the small-molecule drugs enables their antibiotic activity. Section III explores the development of bacterial resistance to antibiotics. The fourth section addresses the molecular logic of antibiotic biosynthesis, starting with regulatory networks that control gene transcription of secondary metabolites in streptomycetes.



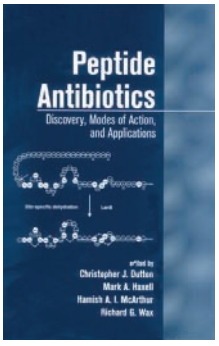
Z700894 Multiple Drug Resistant Bacteria

This book focuses on the problem posed by resistant organisms: multi-resistance. Resistance and multi-resistance arise as consequences of a complex set of biological, social and economic forces. Bacteria gain multi-resistance in a number of ways, gathering individual resistance genes in single genetic elements, activating responses to environmental stress, and growing in biofilms. Two of the most dangerous pathogenic organisms discussed (methicillin-resistant S. aureus and vancomycin-resistant enterococci) pose a threat because they are always multi-resistant. Chapter 7 is devoted to explain a different way to look into the evolution of resistance and a way to search for new antimicrobial drugs.



Z702188 Macrolide Antibiotics: Chemistry, Biology and Practice, 2nd ed.

This book explores the discovery of new macrolide antibiotics, their function, and their clinical use in diseases such as cancer, AIDS, cystic fibrosis and pneumonia. It discusses the creation of synthetic macrolides and the mechanisms of antibiotic activity. The uses for antimicrobial macrolides in clinical practice are also covered. This book is designed to appeal to both the basic and applied research communities interested in microbiology, bacteriology, and antibiotic/antifungal research and treatment.



P1994 Peptide Antibiotics: Discovery, Modes of Action and Applications

This reference summarizes the latest research on the structure, function, and design of synthetic and natural peptide antibiotics, describing practical applications in food preservation and packaging, and in the prevention and treatment of infectious diseases by direct antibacterial action and as part of the adaptive immune response. It discusses these compounds and their applications including: the distribution and classification of diverse, antimicrobial peptides throughout nature, the role in host defense of mucosal surface peptide antibiotics such as defensins and cathepsins, and the genetic basis determining the production of bacterial peptide antibiotics.

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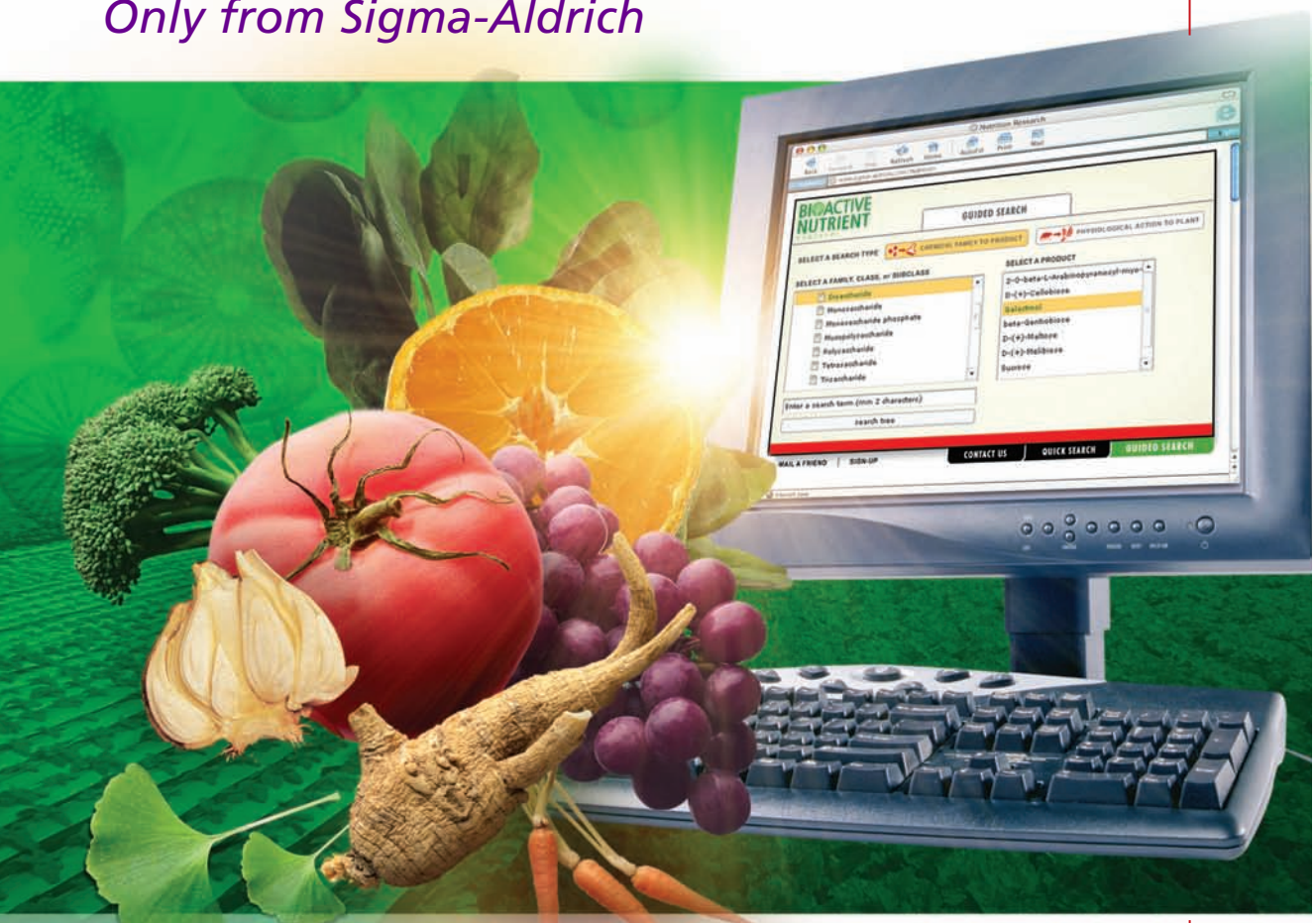

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