

A BRIEF REVIEW OF NUCLEOSIDE ANTIBIOTICS

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Nucleoside antibiotic-producing organisms, extraction methods, biological activities, UV absorption maxima and chemical structures of the nucleoside antibiotics are briefly reviewed in three summary tables. These tables can be conveniently referred to, when screening new metabolites, to determine chemical structures and to study structure-activity relationships of nucleoside antibiotics.

Nucleoside antibiotics are described in order of the aglycone nuclei, namely purine (I-XVIII), pyrrolo(2,3-d)pyrimidine (XIX-XXI), pyrazolo(4,3-d)pyrimidine (XXII-XXIV), pyrimidine (XXV-LVI, LIX, LX), s-triazine (LVII), s-dihydrotriazine (LVIII), imidazole (LXI), pyrazole (LXII), maleimide (LXIII) and 1,3-oxazine (LXIV) in the tables. References of each nucleoside antibiotic are numbered in Table I.

1. Nucleoside Antibiotic-Producing Organisms, Extraction Methods and Biological Activities (Table I)
2. UV Absorption Maxima (Table II)
3. Chemical Structures (Table III)
4. Application of the Summary Tables
 - 4.1 Production of Minimycin by *Str. mediodicidicus*
 - 4.2 A New Nucleoside Antibiotic, Platenocidin

A comprehensive review of nucleoside antibiotics published in 1970 described some 35 nucleosides including 7 biologically inactive substances.¹ More than 29 nucleoside antibiotics have been reported since 1970. Taxonomic studies of producing organisms, extraction methods, antimicrobial spectra and UV spectra of antibiotics are useful for classification or identification of antibiotics, especially in early periods of extraction and purification, to avoid fruitless efforts. The structural diversity in the aglycone base and sugar moieties of nucleoside antibiotics is not independent of the diversity in their biological activities. The diversity of biological activities of nucleoside antibiotics is also related to the diversity in their modes of actions. Thus, classification and identification of nucleoside antibiotics are more complicated than other groups of antibiotics.

1. Nucleoside Antibiotic-Producing Organisms, Extraction Methods and Biological Activities (see Table I)

Most of the nucleoside antibiotics are produced by microbes except for spongosine (XIV), crotonoside (XVII), spongouridine (XXV) and spongothymidine (XXVI). In particular, 55 out of 64 nucleoside antibiotics are produced by *Streptomyces* and many of the nucleoside antibiotics produced by *Streptomyces* contain the curious aglycone or sugar moieties.

Most of the nucleoside antibiotics are hydrophilic in nature and generally adsorbed on active carbon or cation or anion exchange resin from the broth filtrate. The antibiotics adsorbed on active carbon can be eluted with aqueous acetone, acidic methanol or alkaline methanol and active components adsorbed on cation or anion exchange resin can be eluted with aqueous ammonium hydroxide or hydrochloric acid. While herbicidin A and B (XII, XIII), puromycin (XVI), toyocamycin (XX), sangivamycin (XXI), amicetin A, B and C (XXXIX-XLI), oxamicetin (XLII) and bamicetin (XLIII) can be extracted with butanol or amyl acetate from broth filtrates at alkaline pH.

Nucleocidin (III), gougerotin (XXIX), blasticidin S (XXX), amicitin A, B and C (XXXIX-XLI), oxamicetin (XLII) and bamicitin (XLIII) have rather wide antimicrobial spectra compared with those of other nucleoside antibiotics. Those antibiotics and puromycin (XVI) are considered to inhibit protein synthesis.² Generally, each nucleoside antibiotic has a narrow antimicrobial spectrum and inhibits the growth of a few species of some restricted genera of microbes. Nevertheless, biological activities of nucleoside antibiotics are quite different from one another and abound in changes from antibacterial, antiyeast or antifungal to antitumor, antiviral, acaricidal or immunosuppressive characteristics. Cordycepin (II), angustmycins (IV, V), tubercidin (XIX), toyocamycin (XX) and sangivamycin (XXI) are known as inhibitors of nucleotide synthesis.² Though, the -CN group of toyocamycin (XX) is converted to the -CONH₂ group in sangivamycin (XXI), the former inhibits the growth of *Candida* and *Mycobacteria* and the other is effective against *Piricularia* but not against *Candida* and *Mycobacteria*. The mode of action of polyoxins (XLIV-LIII) is inhibition of cell wall synthesis and the antibiotics inhibit the growth of phytopathogenic fungi.⁴

2. UV Absorption Maxima (see Table II)

Nucleoside antibiotics show notable UV absorption maxima in a wide region of 220-320 nm due to individual aglycone moieties and the UV spectra in neutral, acidic and alkaline solutions are quite characteristic for each antibiotic. Thus, the UV spectra and paper chromatogram followed by bioautography are quite useful for identification or structural studies of nucleoside antibiotics.

3. Chemical Structures (see Table III)

Nucleoside antibiotics are composed of an aglycone base and a sugar, but some of nucleosides contain an additional sugar or additional amino acids.

The existence of pyrrolopyrimidine, pyrazolopyrimidine, s-triazine,

s-dihydrotriazine, imidazole, pyrazole, maleimide or 1,3-oxazine nucleus as the aglycone base instead of purine or pyrimidine nucleus is not unusual in nucleoside antibiotics. The unusual C-glycosyl linkage is usual in nucleoside antibiotics containing pyrazolopyrimidine, pyrazole, maleimide or 1,3-oxazine nucleus as the aglycone, while, the N-glycosyl linkage is usual when purine, pyrrolopyrimidine, pyrimidine, s-triazine, s-dihydrotriazine or imidazole nucleus is present as the aglycone except for pseudouridine (LIX) and 1-methylpseudouridine (IX). The C-N bond of the N-glycosyl linkage can be easily hydrolyzed by mild acid to yield the aglycone base and the sugar, while the C-C bond of the C-glycosyl linkage is resistant to acid or alkaline hydrolysis. The aglycone base of formycin A (XXII), 7-aminopyrazolo(4,3-d)-pyrimidine, can be obtained by periodate oxidation of the antibiotic followed by alkaline decomposition and decarboxylation.⁵ The C-C bond of the C-glycosyl linkage is not cleaved by mass spectrometry and the C-nucleoside antibiotics like formycin A (XXII), formycin B (XXIII), pseudouridine (LIX), 1-methylpseudouridine (IX) and showdomycin (LXIII) are characterized by a fragmentation pattern containing a base peak at (m/e) B + 30 due to B-ribose $\longrightarrow$ B-CH=OH⁺, where B is the aglycone moiety.⁶⁻⁸ While the N-nucleoside antibiotics give a base peak at (m/e) B + 1 or B + 2 by mass spectrometry.

The anomeric protons of the C-nucleosides appear at a higher field in the nmr spectra compared to that of the N-nucleosides. The position of the anomeric proton of formycin A (XXII) or pseudouridine (LIX) is at 5.14 or 4.72 ppm respectively, whereas the position of the anomeric proton of adenosine or uridine is 6.15 or 6.0 ppm respectively.⁸⁻¹⁰

Septacidine (XV) has an extraordinary structure for a nucleoside antibiotic having N⁶-glycosyl adenine, L-septose as an uncommon seven-carbon sugar and isopalmitic acid as an unusual acyl moiety.

D-Ribose and 3-deoxy- (II), 4-fluoro- (III), 3-amino-3-deoxy- (VI-IX, XVI) and 2-amino-2-deoxy- (XVIII) derivatives of D-ribose are widely distributed as the sugar moieties in the nucleoside antibiotics. Aristeromycin (XI) contains the carbocyclic analogue of D-ribose. D-Arabinose (X, XXV, XXVI), angustose (IV), D-psicose (V) and the carboxyamino sugar in polyoxins (XLIV-LV) are also present as furanoses in the antibiotics to form the N-glycosyl linkage. L-Septose (XV), the sugar in aspiculamycin or gougerotin (XXVIII, XXIX), the sugar in blasticidin S (XXX), amicitose (XXXIX, XL, XLIII) and 3-hydroxyamicitose (XLII) are involved as pyranoses to form the N-glycosyl linkage. 3-Amino-3-deoxy-D-glucose (XXVII), ezoaminuroic acid (XXXI-XXXVIII), amosamine (XXXIX, XL, XLII) and 4,6-dideoxy-4-methylamino-D-glucose (XLIII) are also pyranoses as the additional sugars of the nucleoside antibiotics to form the O-glycosyl linkage. 3',7'-Anhydro-5'-deoxy-5'-amino-D-threo-D-allo-octafuranuroic acid in ezomycins (XXXI-XXXVI) and the sugar in herbicidins (XII, XIII) are unique sugars in having both furanose and pyranose structures.

The β -N- or β -C-glycosyl structure can be essential for the nucleoside antibiotics to show biological activities with the exception of septacidin (XV).¹¹ Ezomycin C₂ (XXXVI) having the α -N-glycosyl linkage is an artifact from ezomycin B₂ (XXXIV) having the β -N-glycosyl linkage or D₂ (XXXVIII).¹² Thus, ezomycin C₁ (XXXV) having the α -N-glycosyl linkage may also be an artifact from ezomycin B₁ or D₁ (XXXIII, XXXVII). To the present, no other nucleoside antibiotic has been reported to have the α -N- or α -C-glycosyl linkage or to contain L-sugar similar to septacidin (XV).

4. Application of the Summary Tables (see Table I, II and III)

Though 1- β -D-arabinofuranosylcytosine (Ara-C) has not yet been isolated as a natural product, the structure of Ara-C synthesized is closely related to that of spongadenosine, spongouridine and spongothymidine (X, XXV, XXVI).¹³ Ara-C is effective against neoplasms in mice, rats and human¹⁴ and used

Table I. Producing Organisms, Extraction Methods and Biological Activities of Nucleoside Antibiotics

Antibiotic	Producing Organism	Extraction Method	Biological Activity (primarily active against)
1 Nebularine 15-17 (9- β -D-Ribofuranosylpurine)	<i>Agaricus nebularis</i> <i>Str. yokosukanensis</i>	adsorbed on carbon, eluted with 70 % aqu. Me ₂ CO at pH 2	Mycobacteria, Sarcoma 180
2 Cordycepin 18, 19 (3'-Deoxyadenosine)	<i>Cordyceps militaris</i> <i>Aspergillus nidulans</i>	adsorbed on carbon, eluted with Me ₂ CO	Bacillus, Ehrlich ascites tumor
3 Nucleocidin 20-23	<i>Str. calvus</i>	adsorbed on Darco G 60-celite 545 at pH 7, eluted with 95 % aqu. Me ₂ CO or acidic EtOH	Gram +, -, Mycobacteria, Endamoeba, Trypanosoma
4 Angustmycin A 24-27 (Decoynine)	<i>Str. hygrosopicus</i>	adsorbed on carbon at pH 7.6, eluted with 80 % aqu. Me ₂ CO at pH 2	Mycobacteria
5 Angustmycin C (Psicofurarine)			"
6 3'-Amino-3'-deoxy- 28-30 adenosine	<i>Helminthosporium</i> <i>Cordyceps militaris</i> <i>Aspergillus nidulans</i>	adsorbed on Dowex-50-H ⁺ , eluted with NH ₄ Cl	Cryptococcus, Candida, Ehrlich ascites tumor
7 3'-Acetoamido-3'- 31, 32 deoxyadenosine	<i>Helminthosporium</i>	adsorbed on Dowex-50-NH ₄ ⁺ , eluted with 0.5 N NH ₄ OH	none
8 Homocitrullyamino- 33, 34 adenosine	<i>Cordyceps militaris</i>	extracted from mycelia with MeOH	Inhibition of protein synthesis of cell- free extracts of <i>E. coli</i> or rat liver
9 Lysylaminoadenosine 35	<i>Cordyceps militaris</i>	adsorbed on Dowex-50-NH ₄ ⁺ , eluted with 3 N NH ₄ OH	
10 Spongoadenosine 36-38 (Ara-A, 9- β -D-Arabino- furanosyladenine)	<i>Str. antibioticus</i>	adsorbed on carbon, eluted with 50 % aqu. Me ₂ CO	DNA virus
11 Aristeromycin 39-41	<i>Str. citricolor</i>	adsorbed on carbon at pH 8, eluted with 80 % aqu. Me ₂ CO	Xanthomonas, Piricularia
12 Herbicidin A 42-44	<i>Str. saganonensis</i>	adsorbed on Duolite S-30, eluted with 50 % aqu. Me ₂ CO	Trichophyton, Candida, Pellicularia
13 Herbicidin B			"
14 Spongosine 45	<i>Cryptotechia crypta</i>	extracted from mycelia with Me ₂ CO	none
15 Septacidin 46, 47	<i>Str. fimbriatus</i>	extracted from mycelia with aqu. BuOH	Trichophyton, Fusarium, Adenocarcinoma
16 Puromycin 48, 49	<i>Str. alboniger</i>	extracted with n-BuOH at pH 9-9.5	Gram +, Tripanosoma, Virus, HeLa cell
17 Crotonoside 50, 51	<i>Croton tiglium</i>	extracted of ground seeds with MeOH	none
18 2'-Amino-2'-deoxy- 52, 53 guanosine	<i>Aerobacter</i>	adsorbed on IRC-50, eluted with 0.5 N NH ₄ OH	<i>E. coli</i> KY 8323, HeLa cell, Sarcoma 180

19	Tubercidin 54, 55	Str. tubercidicus	adsorbed on carbon, eluted with acidic aqu. Me ₂ CO	Mycobacteria, Candida, Tumor
20	Toyoamycin 56-58	Str. toyoensis	adsorbed on Ionex-C-H ⁺ , eluted with 80 % aqu. Me ₂ CO	Mycobacteria, Candida, HeLa cell
21	Sangivamycin 59-61	Str. purpureofuscus	adsorbed on carbon, eluted with acidic MeOH	Leukemia I1210, HeLa cell, Piriularia
22	Formycin A 62-66	Nocardia interforma	adsorbed on carbon at pH 7, eluted with 50 % aqu. MeOH or 50 % aqu. Me ₂ CO	Mycobacteria, Xanthomonas, Leukemia I1210, HeLa cell
23	Formycin B (Lauridin)	Nocardia interforma Str. lauridulae		Xanthomonas
24	Oxofornycin B 66, 67			none
25	Spongouridine 68	Cryptotethia crypta	Dried sponges are extracted with Me ₂ CO	none
26	(Ara-U, 1-β-D-Arabinofuranosyluracil) 69, 70			
27	Spongouridine (Ara-U, 1-β-D-Arabinofuranosylthymine) 71, 72	Streptomyces	adsorbed on IRC-50, eluted with 0.5 N NH ₄ OH	Pseudomonas, Alternaria
28	Aspiculamycin 73-75	Str. toyoensis	adsorbed on IRC-50-H ⁺ , eluted with 1 N NH ₄ OH	anthelmintic, acaricidal
29	Gougerotin 76, 77	Str. gougerotii	adsorbed on IRC-50-Na, eluted with 0.5 N HCl	Gram +, -, Mycobacteria
30	Blasticidin S 78-82	Str. griseochromogenes Str. more-okaensis	adsorbed on IRC-50-Na, eluted with 0.5 N HCl	Gram +, -, Piriularia
31	Ezomycin A ₁ 12, 83-86	Str. kitazawaensis	adsorbed on Dowex 1 X 1, eluted with 0.5 N HCl	Salerotinia, Botrytis
32	Ezomycin A ₂			none
33	Ezomycin B ₁			Sclerotinia, Botrytis
34	Ezomycin B ₂			none
35	Ezomycin C ₁			"
36	Ezomycin C ₂			"
37	Ezomycin D ₁			"
38	Ezomycin D ₂			"
39	Amicetin A 87-93	Str. viraceus-drappus Str. fasciculatus Str. sacromyocetius	adsorbed on IRC-50-H ⁺ or IR 100, eluted with acidic 80 % aqu. Me ₂ CO	Gram +, Mycobacteria
40	Amicetin B (Plicacitin)	Str. viraceus-drappus Str. plicatus	extracted with BuOH or AcOEt at pH 7-8.5	"
41	Amicetin C	Str. viraceus-drappus	extracted with AcOH at pH 7-8.5	"
42	Oxamicetin 94-96	Arthrobacter oxamicetus	extracted with BuOH at pH 8.2-8.4	Gram +, -, Mycobacteria

43	Banicetin 97, 98	Str. plicatus		extracted with BuOH at pH 7.1-8.6	Gram +, Mycobacteria
44	Polyoxin A 99-103	Str. cacaoi		adsorbed on carbon at pH 2, eluted with 60 % aq. Me ₂ CO	Alternaria, Cochliobolus, Piricularia
45	Polyoxin B			"	"
54	Polyoxin C			none	none
49	Polyoxin G			adsorbed on carbon, eluted with 50 % aq. Me ₂ CO	Alternaria, Cochliobolus, Piricularia
55	Polyoxin I			"	none
50	Polyoxin H			"	Alternaria, Cochliobolus, Piricularia
51	Polyoxin J			"	"
46	Polyoxin D			"	"
47	Polyoxin E			"	"
48	Polyoxin F			"	"
52	Polyoxin K			"	"
53	Polyoxin L			"	"
56	Nikkomycin 104	Str. tendae		adsorbed on Dowex 50W X 4-Na, eluted with 0.01 N NH ₄ OH	Phytopathogenic fungi
57	5-Azacytidine 105, 106	Streptovercillium ladakanus		adsorbed on Darco G-60, eluted with 50 % aq. Me ₂ CO	Gram -, Leukemia L1210, Ehrlich ascites tumor
58	U-44590 8	Str. platensis			
59	Pseudouridine 8, 107	Str. hygroscopicus		adsorbed on IRA-400, eluted with 0.4 N HCl	none
		Agrobacterium tumefaciens			
60	1-Methylpseudouridine 8)	Str. platensis		adsorbed on CAL-carbon, eluted with 75 % aq. Me ₂ CO	Gram +, -, Herpes virus
61	Bredinin 108	Eupenicillium brefeldianum		adsorbed on IRA 411-OH ⁻ , eluted with 2 % aq. AcOH	Cardida, Vaccinia virus, Immunosuppressive
62	Pyrazonycin 109	Str. cardidus		adsorbed on carbon, eluted with 50 % aq. Me ₂ CO	Rhino, Measles, Herpes, Simplex and Vaccinia virus
63	Showdomycin 10, 110, 111	Str. showdoensis		adsorbed on carbon at pH 5, eluted with 80 % aq. Me ₂ CO	Gram +, -, Ehrlich ascites tumor
64	Mindimycin 112-114 (Oxazimycin)	Str. hygroscopicus Str. tatesashirensis		adsorbed on carbon at pH 2, eluted with 50 % aq. Me ₂ CO	Gram +, -, Ehrlich ascites tumor, Sarcoma 180

Str. = Streptomyces, Gram + = Gram positive bacteria, Gram - = Gram negative bacteria

Table II. Ultraviolet Absorption Maxima of Nucleoside Antibiotics

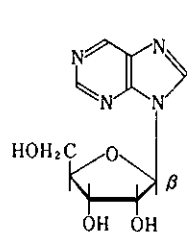
Antibiotic	λ_{max} neutral (nm)	λ_{max} acid (nm)	λ_{max} alkaline (nm)
1 Nebularine (9- β -D-Ribofuransylpurine)		262 (E, 232)	263 (E, 361)
2 Cordycepin (3'-Deoxyadenosine)		260 (e, 14400)	260 (e, 14600)
3 Nucleocidin	256 (e, 15500)	255-257 (E, 392)	259 (E, 406)
4 Angustmycin A (Deocynine)	260 (E, 570)	260 (e, 17100)	260 (e, 17100)
5 Angustmycin C (Fisicofuranine)		259 (E, 508)	261 (E, 527)
6 3'-Amino-3'-deoxyadenosine	260 (e, 17300)		
7 3'-Acetoamido-3'-deoxyadenosine	260 (e, 15600)		
8 Homocitrullylamroadenosine			
9 Lysylamroadenosine			
10 Sporgoadenosine (Ara-A, 9- β -D-Arabino- furanosyladenine)	259 (e, 13400)	257.5 (e, 12700)	259 (e, 14000)
11 Aristeromycin	262 (E, 555)	262 (E, 555)	262 (E, 555)
12 Herbicidin A	258 (e, 11500 in MeOH)		
13 Herbicidin B	258 (e, 9200 in MeOH)		
14 Spongiosine	267 (e, 12500)	249 (e, 8350), 274 (e, 11900)	268 (e, 12700)
15 Septacidin	264 (E, 253 in MeOH)		272 (E, 275)
16 Purumycin		267.5 (E, 195)	275 (E, 203)
17 Crotonoside	230 (e, 6000), 270 (e, 10500)	235 (e, 9000), 285 (e, 9000)	240 (e, 4000), 275 (e, 7500)
18 2'-Amino-2'-deoxyguanosine	252 (e, 14100), 275 (sh, e, 9500)	255 (e, 12500), 278 (sh, e, 8500)	258 (e, 12000), 267 (e, 12100)
19 Tubercidin		227 (e, 25200), 270 (e, 12200)	270 (e, 12100)

20	Toyocamycin	230 (E, 400), 277 (E, 548)	235 (E, 760), 273 (E, 563)	233 (E, 398), 280 (E, 571)
21	Sangivamycin	229 (e, 8200 in EtOH), 278 (e, 15100 in EtOH)	228 (e, 9500), 273 (e, 12800)	227 (e, 14100), 277 (e, 14400)
22	Formycin A	295 (E, 380)	234 (E, 280), 295 (E, 340)	235 (E, 500), 305 (E, 260)
23	Formycin B (Laurusin)	280 (E, 294)	221 (E, 543), 276 (E, 300)	230 (E, 643), 292 (E, 338)
24	Oxoformycin B	288 (e, 395)	288 (E, 220)	304 (E, 168)
25	Spongouridine (Ara-U, 1- β -D-Arabinofuranosyl- uracil)	265 (e, 9300)	265 (e, 9300)	236 (e, 8250), 268 (e, 8600)
26	Spongothymidine (Ara-T, 1- β -D-Arabinofuranosyl- thymine)	270 (e, 9200)	270 (e, 6800)	270 (e, 7600)
27	Hikiijimycin	266 (e, 5600)	274 (e, 8000)	268 (e, 5500)
28	Aspiculamycin	236 (e, 8250), 268 (e, 8600)	276 (e, 11300)	236 (e, 8250), 268 (e, 8600)
29	Gougerotin	228 (e, 8900), 269 (e, 9400)	276 (e, 13300)	228 (e, 8900), 269 (e, 9600)
30	Blasticidin S		275 (e, 14300)	266-270 (e, 9450)
31	Ezomycin A ₁		278 (e, 10500)	271 (e, 7900)
32	Ezomycin A ₂		278 (e, 11100)	229 (e, 6100), 271 (e, 7100)
33	Ezomycin B ₁		262 (e, 7000)	286 (e, 6100)
34	Ezomycin B ₂		261.5 (e, 6300)	286 (e, 4900)
35	Ezomycin C ₁		263 (e, 6400)	287 (e, 4900)
36	Ezomycin C ₂		263.5 (e, 6200)	287 (e, 4800)
37	Ezomycin D ₁		263.5 (e, 6900)	287 (e, 5200)
38	Ezomycin D ₂		264 (e, 6700)	287 (e, 4900)
39	Amicetin A	305 (E, 465)	316 (E, 433)	322 (E, 470)
40	Amicetin B (Plicacetin)	249 (a, 26.6), 321 (a, 53.5)	257 (a, 36.8), 311.5 (a, 29.2)	329 (a, 63.9)
41	Amicetin C	257 (E, 288), 304 (E, 250)	255 (E, 183), 313 (E, 332)	274 (E, 174), 318 (E, 217)

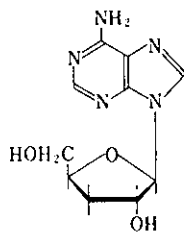
42 Oxamidoetin	305 (e, 31700)	316 (e, 26600)	322 (e, 21900)
43 Bamicitin	302 (a, 45.5)	314 (a, 43.7)	322 (a, 52.5)
44 Polyoxin A		262 (E, 142)	264 (E, 103)
45 Polyoxin B		262 (E, 172)	264 (E, 130)
54 Polyoxin C		262 (E, 297)	264 (E, 231)
49 Polyoxin G		262 (E, 170)	264 (E, 134)
55 Polyoxin I		262.5 (E, 165)	264 (E, 123)
50 Polyoxin H		262 (E, 127)	266 (E, 103)
51 Polyoxin J		264 (log e, 3.91)	267 (log e, 3.81)
46 Polyoxin D		218 (E, 217), 276 (E, 127)	271 (E, 137)
47 Polyoxin E		218 (E, 200)	271 (E, 128)
48 Polyoxin F		218 (E, 200), 276 (E, 200)	271 (E, 118)
52 Polyoxin K		259 (log e, 3.95)	267 (log e, 3.86)
53 Polyoxin L		259 (log e, 3.96)	262 (log e, 3.85)
56 Nikkomycin		225 (sh, a, 0.88), 290 (a, 1.5)	242 (a, 1.58), 305 (a, 1.0)
57 5-Azacytidine	241 (e, 8767)	249 (e, 3077)	223 (e, 24200)
58 U-44590			
59 Pseudouridine	262 (e, 8470)	262 (e, 8390)	286 (e, 8400)
60 1-Methylpseudouridine	209 (e, 7546), 270 (e, 9081)	209 (e, 10342), 270 (e, 8923)	267 (e, 6192)
61 Brdinin	245 (E, 250), 279 (E, 580)	245 (E, 260), 281 (E, 495)	277 (E, 660)
62 Pyrazomycin	263 (e, 6200)		307 (e, 8100)
63 Showdomycin	220-221 (E, 442)		
64 Minimycin (Oxazinomycin)		230 (E, 188)	

E=E $\frac{1\%}{1\text{ cm}}$, e=Molecular extinction, a=Absorption, sh=Shoulder

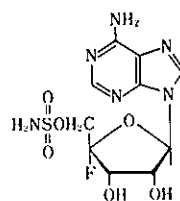
Table III. Chemical Structures of Nucleoside Antibiotics



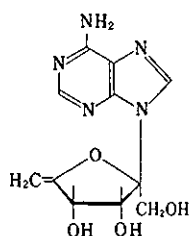
(I) Nebularine



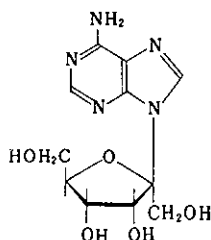
(II) Cordycepin



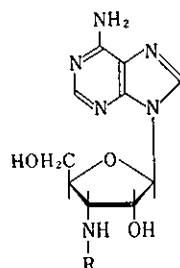
(III) Nucleocidin



(IV) Angustmycin A



(V) Angustmycin C



(VI) 3'-Amino-3'-deoxy-adenosine

R=H

(VII) 3'-Acetoamido-3'-deoxy-adenosine

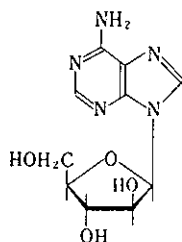
R=COCH₃

(VIII) Homocitrullylamino-adenosine

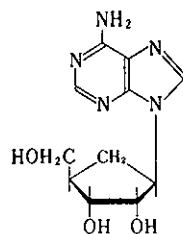
R=COCHCH₂CH₂CH₂CH₂NHCONH₂

(IX) Lysylaminoadenosine

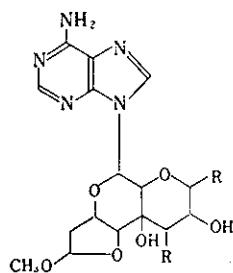
R=COCHCH₂CH₂CH₂CH₂NH₂



(X) Spongadenosine



(XI) Aristeromycin



(XII) Herbicidin A

R= H₃C-C(=O)-CH₂OH, R'=COOCH₃

or

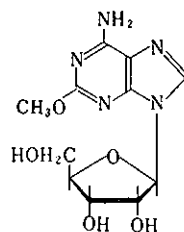
R=COOCH₃, R'= H₃C-C(=O)-CH₂OH

(XIII) Herbicidin B

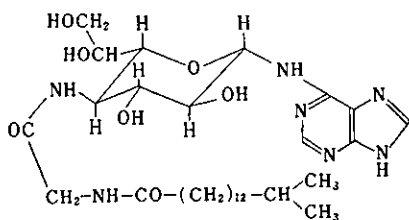
R=OH, R'=COOCH₃

or

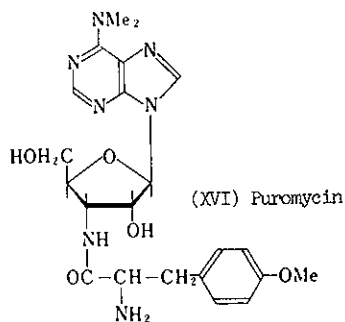
R=COOCH₃, R'=OH



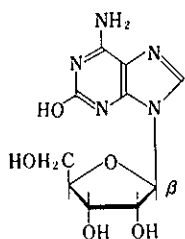
(XIV) Spongine



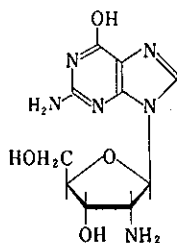
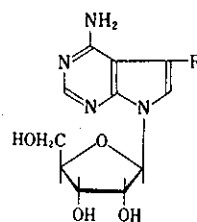
(XV) Septacidin



(XVI) Puromycin



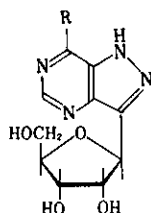
(XVII) Crotonoside


(XVIII) 2'-Amino-2'-deoxy-
guanosine


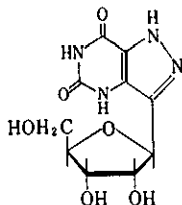
(XIX) Tubercidin, R=H

(XX) Toyocamycin, R=-CN

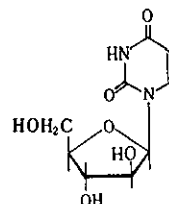
(XXI) Sangivamycin, R=-CONH2


(XXII) Formycin A, R=-NH₂

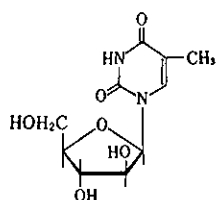
(XXIII) Formycin B, R=-OH



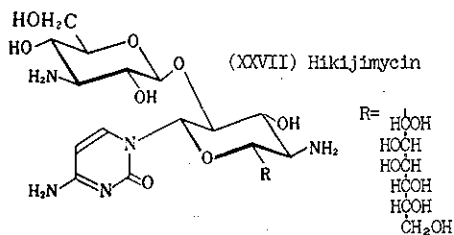
(XXIV) Oxoformycin B



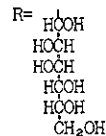
(XXV) Spongouridine

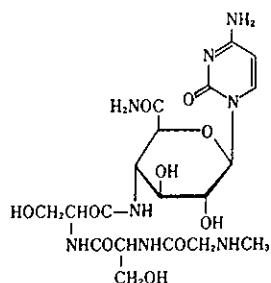


(XXVI) Spongothymidine

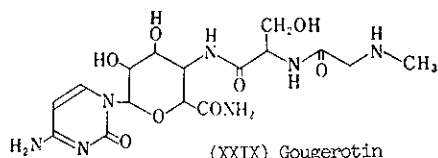


(XXVII) Hikijimycin

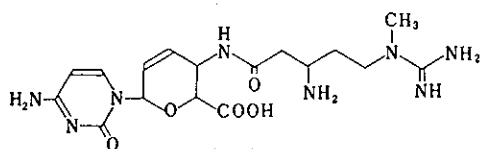




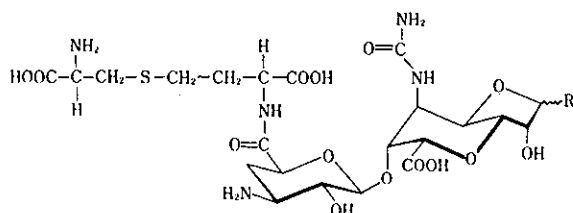
(XXVIII) Aspiculamyacin



(XXIX) Gougerotin



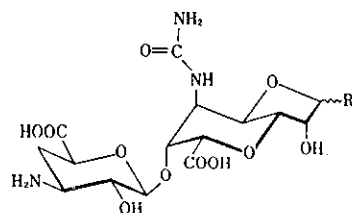
(XXX) Blastidicin S



(XXXI) Ezomycin A₁, R=β-1-Cytosine

(XXXIII) Ezomycin B₁, R=β-5-Uracil

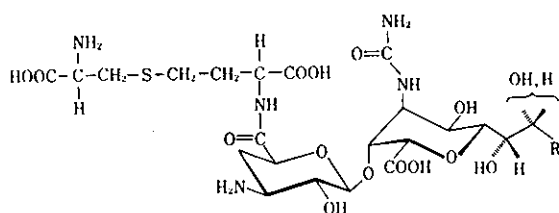
(XXXV) Ezomycin C₁, R=α-5-Uracil



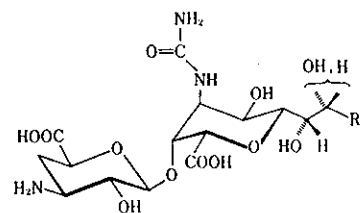
(XXXII) Ezomycin A₂, R=β-1-Cytosine

(XXXIV) Ezomycin B₂, R=β-5-Uracil

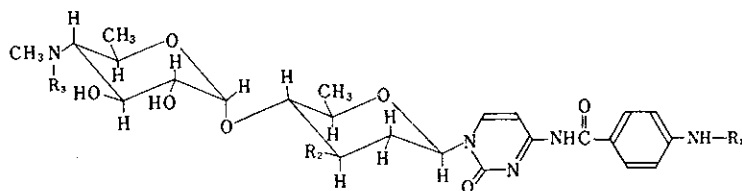
(XXXVI) Ezomycin C₂, R=α-5-Uracil



(XXXVII) Ezomycin D₁, R=5-Uracil



(XXXVIII) Ezomycin D₂, R=5-Uracil



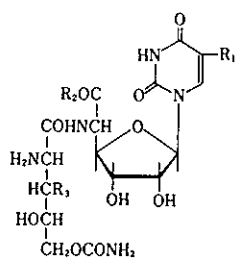
(XXXIX) Amicetin A; R₁=CO-C(CH₃)₂-CH₂OH, R₂=-H, R₃=-CH₃

(XL) Plicacetin; R₁=-H, R₂=-H, R₃=-CH₃

(XLI) Amicetin C; ?

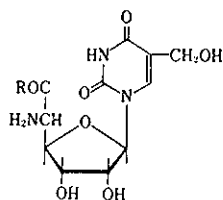
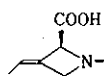
(XLII) Oxamicetin; R₁=CO-C(CH₃)₂-CH₂OH, R₂=-OH, R₃=-CH₃

(XLIII) Bamicetin; R₁=CO-C(CH₃)₂-CH₂OH, R₂=-H, R₃=-H


Polyoxin R₁ R₂ R₃

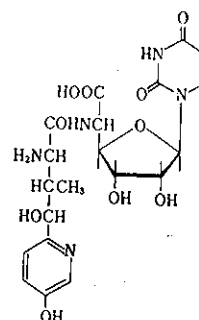
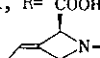
(XLIV)	A	-CH ₂ OH	POAM	-OH
(XLV)	B	-CH ₂ OH	-OH	-OH
(XLVI)	D	-COOH	-OH	-OH
(XLVII)	E	-COOH	-OH	-H
(XLVIII)	F	-COOH	POAM	-OH
(XLIX)	G	-CH ₂ OH	-OH	-H
(L)	H	-CH ₃	POAM	-OH
(LI)	J	-CH ₃	-OH	-OH
(LII)	K	-H	POAM	-OH
(LIII)	L	-H	-OH	-OH

POAM: Polyoximic acid moiety



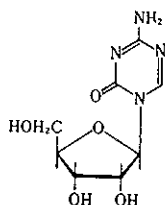
(LIV) Polyoxin C, R=-OH

(LV) Polyoxin I, R=COOH

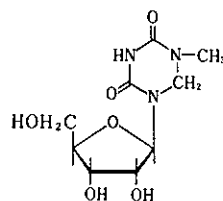


(LVI) Nikkomycin

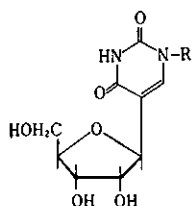
(Configuration of the sugar moiety is not yet determined.)



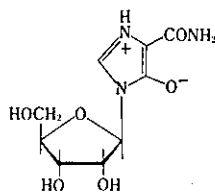
(LVII) 5-Azacytidine



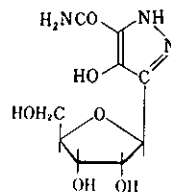
(LVIII) U-44590



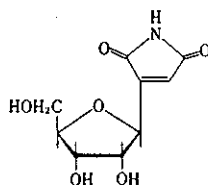
(LIX) Pseudouridine, R=-H

(LX) 1-Methylpseudouridine
R=-CH₃


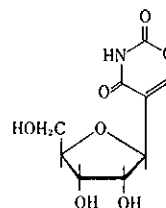
(LXI) Bredinin



(LXII) Pyrazomycin



(LXIII) Showdomycin



(LXIV) Minimycin

clinically in cancer chemotherapeutics. The nucleoside antibiotics are interesting to study for structure-activity relationships, because of their diversity in chemical structures as well as in biological activities.

Application of the summary tables is described as follows.

4.1 Production of Minimycin by *Str. medicidicus*¹¹⁵

Culture broth of *Str. H 86-NSY-6* identified as *Str. medicidicus* was shown to produce an antibiotic inhibiting *E. coli* K-12 ML 1629 which was known to be resistant to aminocyclitol antibiotics. The antibiotic was adsorbed on active carbon from the broth filtrate at pH 2. The antibiotic adsorbed on carbon was eluted with 80 % aqueous acetone at pH 7 and the acetone was removed in vacuo. The active component was further adsorbed on Amberlite IRA-400 (OH⁻-type) and eluted with H₂O at pH 2. The active eluate was lyophilized after neutralization with dil. NH₄OH to recover the crude antibiotic. The crude antibiotic was purified by column chromatography on Avicel (microcrystalline cellulose) developed with n-BuOH:acetone:H₂O=4:1:1 after gel filtration on Sephadex G-15 eluted with H₂O and following gel filtration on Sephadex LH 20 eluted with MeOH. The pure antibiotic was recovered by recrystallization from n-BuOH as white plates, decomp. p., 161.5-165.0°.

UV; $\lambda_{\text{max}}^{\text{MeOH}} = 232 \text{ nm}$ ($E_{1\%}^{1\text{cm}} = 184$).

The antibiotic inhibits the growth of restricted species of Gram positive and negative bacteria by the agar dilution method. The antibiotic shows an inhibition zone by the cylinder agar plate method against *E. coli* K-12 ML 1629, while the antibiotic is inactive against the same bacteria by the agar dilution method.

Extraction method, biological activity and UV spectrum of the antibiotic are identical with that of minimycin (LXIV). The antibiotic was confirmed to be minimycin by comparing the bioautograms and IR spectra of the antibiotic and minimycin. *Str. hygrosopicus* and *Str. tanesashinensis* are known to

produce minimycin (see Table I). Thus, this is the first report on the production of minimycin by *Str. mediocidicus*.

4.2 A New Nucleoside Antibiotic, Platenocidin ¹¹⁶

Culture broth of *Str. H 273-NSY-2*, identified as *Str. platensis* ¹¹⁷ was shown to produce an antibiotic effective only against *Candida* but not against other yeasts, fungi or bacteria. The antibiotic can be neither extracted with *n*-BuOH nor adsorbed on active carbon from the broth filtrate. The antibiotic can be adsorbed on Amberlite IR 120 (H^+ -form) and eluted with 1 N NH_4OH followed by lyophilization to yield the crude antibiotic. A small amount of the crude antibiotic was purified by paper chromatography followed by elution and lyophilization. The purified antibiotic showed a UV spectra quite similar to that of polyoxin A, B, C and G (XLIV, XLV, LIV, XLIX). Nevertheless, polyoxins are inactive against *Candida*. While *Str. platensis* is known to produce the nucleoside antibiotics, namely U-44590 (LVIII), pseudouridine (LIX) and 1-methylpseudouridine (LX) (see Table I), physico-chemical and biological properties of the antibiotic produced by *Str. H 273-NSY-2* are differentiated from those antibiotics. Thus, the antibiotic produced by *Str. H 273-NSY-2* can be considered to be a new nucleoside antibiotic and is named platenocidin, relating it to the antibiotic-producing microbe.

Platenocidin is amphoteric in nature and purified by DEAE-Sephadex A-25 column chromatography eluted with 0.1 M of pyridine-acetate buffer (pH 4.8), gel filtration on Sephadex G-10 column eluted with 0.05 M of the same buffer, SP-Sephadex column chromatography eluted with 0.02 M of the same buffer and finally DEAE-Sephadex A-25 column chromatography eluted with 0.05 M of the same buffer. The pure antibiotic was obtained as white amorphous powder, decomp. p., 117-120°. Elementary microanalysis gave C, 43.03; H, 4.73; N, 15.62 % and no halogen or sulfur was observed.

UV; $\lambda_{\max}$ ($E \frac{1}{1} \%$), 255 nm (216) in H_2O , 260 nm (257) in 0.1 N HCl and 257 nm (230) in 0.1 N NaOH. The UV spectra of platenocidin are quite similar to those of polyoxin A (XLIV) except for higher extinction, but the papergram of platenocidin does not accord with that of polyoxins. Though the structure has not yet been fully elucidated, nikkomycin (LVI) can be considered to be closely related to polyoxins. Nevertheless, the UV maxima of nikkomycin can be differentiated from that of platenocidin.

The existence of 5-hydroxymethyluracil in platenocidin is suggested from the UV spectra and 5-hydroxymethyluracil is obtained by mild acid hydrolysis of platenocidin. Thus, platenocidin can be considered to be a new nucleoside antibiotic having 5-hydroxymethyluracil as the aglycone and the N-glycosyl linkage. The structure of platenocidin is now under investigation and progress in its elucidation will be reported in the future.

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