A DICTIONARY OF ANTIBIOSIS

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Compiled by LEONARD KAREL

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and

ELIZABETH SPENCER ROACH

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FOREWORD

SINCE its inception, the Division of Research Grants and Fellowships of the National Institutes of Health has endeavored whenever possible and feasible to fulfill its prime objectives of coordination, promotion, and stimulation of research, particularly in neglected areas. It is the earnest belief of the Experimental Therapeutics Study Section that in this *Dictionary of Antibiosis* lies a gratifying measure of achievement of part of these objectives as related to a small but nevertheless significant facet of medical research.

It is hoped that this volume will attain the usefulness envisioned for it and that it will be a source of real assistance to those who may choose to use it.

WALSH MCDERMOTT, *Chairman*
Experimental Therapeutics Study Section
National Institutes of Health

PREFACE

FOR THE PURPOSES of this dictionary the term antibiotic is defined as a substance derivable from living organisms and capable of adversely modifying the vital functions of specific microorganisms. The data included are arranged alphabetically and consist of (1) compilation of substances tested for antibiotic activity; (2) available information on source, extraction, chemical and physical properties, spectrum *in vitro* and *in vivo,* toxicological and pharmacological, clinical and experimental clinical results; and (3) enumeration of organisms (designated as test organisms) against which substances have been tested for antibiotic activity. Under each of the test organisms there are given, wherever applicable, the species tested against it for antibiosis, and the named antibiotics similarly tested against it or, where very long lists of substances have been tested for antibiosis and appear in one paper, the bibliographic reference only.

The bibliography is arranged alphabetically, according to authors, with appropriate cross-references, and cites the complete title of each paper recorded.

It has not been practicable routinely to include strain designations. For precise information regarding these designations, the bibliographic references to the individual species should be consulted.

Neither has it been practicable to include two of the older antibiotics—ethyl alcohol and quinine, and only brief sketches have been given for penicillin and streptomycin, both of which have been adequately covered by other authors.

L.K.
E.S.R.

Bethesda, Maryland
February 1, 1951

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CONTENTS

A DICTIONARY OF ANTIBIOSIS

ABBREVIATIONS AND EXPLANATIONS

aff.—*affinis*
b.p.—blood pressure
cc—cubic centimeter(s)
cf.—compare
corr.—corrected
decomp.—decomposes
f.—*forma*
gm—gram(s)
higher plant—refers to seed-producing plants and to ferns
hr—hour(s)
i.m.—intramuscular
in—inch
inj(s)—injection(s)
i.p.—intraperitoneal
i.v.—intravenous
kg—kilogram(s)
l—liter(s)
lb—pound(s)
LD_{50}—median lethal dose
mg—milligram(s)
min—minutes
ml—milliliter(s)
M.L.D.—minimum lethal dose, median lethal dose
mo—month(s)
mol. wt.—molecular weight
m.p.—melting point
M.T.D.—minimum toxic dose; maximum therapeutic dose; maximum tolerated dose
n.sp. or n.spp.—new species
p.o.—*per os*
ppm—parts per million (equivalent to 1 microgram per cc)
rm. temp.—room temperature
s.c.—subcutaneous
sp.—species (singular)
spp.—species (plural)
uncorr—uncorrected
v. or var.—variety
wk—week(s)
wt.—weight
yr—year(s)

A

Abelia floribunda, a higher plant, aqueous extracts of which are effective *in vitro* against *Staphylococcus aureus* but not against *Escherichia coli.* See Osborn, 1943.

Abelia gardneri, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Abelia schumannii, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Aberia caffra, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Abies religiosa, a higher plant, aqueous extracts of the commercial wood of which are ineffective *in vitro* against *Staphylococcus aureus, Escherichia coli,* and *Bacillus anthracis.* See Sanchez et al., 1948.

Abrus precatorius, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

abscesses, clinical, see BACITRACIN; GRAMICIDIN S; PENICILLIN; STREPTOMYCIN; TYROTHRICIN.

Absidia glauca, a fungus, the culture media of which are ineffective *in vitro* against *Staphylococcus aureus, Escherichia coli,* and *Pseudomonas aeruginosa.* See Wilkins and Harris, 1943a.

Absidia orchidis, a fungus which gives doubtful results when tested *in vitro* against *Escherichia coli* and *Staphylococcus aureus.* See Robbins et al., 1945.

Absidia ramosa, a fungus which gives doubtful results when tested *in vitro* against *Escherichia coli* and *Staphylococcus aureus.* See Robbins et. al., 1945.

Abutilon "boule de neige," a higher plant, aqueous extracts of the garden hybrid of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Abutilon striatum, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Abutilon thompsonii, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acacia jurema, a higher plant, extracts of which are ineffective *in vitro* against *Staphylococcus aureus, Escherichia coli,* and *Proteus* X-19. See Cardoso and Santos, 1948.

Acacia podalyriaefolia, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acacia verticillata, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acaena adscandens, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acaena myriophylla, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acalypha cancana, a higher plant, aqueous extracts of which are effective *in vitro* against *Staphylococcus aureus* but not against *Escherichia coli.* See Osborn, 1943.

Acalypha hamiltoniana, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acalypha hispida, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acalypha macrostachya, a higher plant, aqueous extracts of which are effective *in vitro* against *Staphylococcus aureus* but not against *Escherichia coli.* See Osborn, 1943.

Acalypha montevidiensis, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acalypha virginica, a higher plant, extracts of which are ineffective *in vitro* against *Bacillus subtilis* and *Escherichia coli.* See Sanders et al., 1945.

Acalypha wilkesiana, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acalypha wilkesiana v. **macafeana,** a higher plant, aqueous extracts of which are effective *in vitro* against *Staphylococcus aureus* but not against *Escherichia coli.* See Osborn, 1943.

Acantholimon glumaceum, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acanthopanax simonii, a higher plant, aqueous extracts of which are effective *in vitro* against *Staphylococcus aureus* but not against *Escherichia coli.* See Osborn, 1943.

Acanthopyrus sp., a higher plant, aqueous extracts of which show little or no inhibition of growth when tested *in vitro* against *Staphylococcus aureus, Escherichia coli, Erwinia carotovora,* and *Phytomonas tumefaciens.* See Hayes, 1947.

Acanthorhynchus vaccinii. 1 See ACTINOMYCES ANNULATUS; ACTINOMYCES FLAVOVIRENS; ACTINOMYCES GOUGEROTI; ACTINOMYCES HALSTEDII; ACTINOMYCES MADURAE; ACTINOMYCES VIRIDOCHROMOGENUS. **2** As test organism *in vitro,* see Alexopoulos and Herrick, 1942 (actinomycetes).

Acanthospermum xanthoides, a higher plant, extracts of which are ineffective against experimental malaria. See Spencer et al., 1947.

Acanthus montanus, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acanthus niger, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acer negundo, a higher plant, extracts of which are ineffective *in vitro* against *Bacillus subtilis* and *Escherichia coli.* See Sanders et al., 1945.

Acer plantanoides, a tree, extracts of which are ineffective *in vitro* against *Staphylococcus aureus, Escherichia coli,* and *Mycobacterium tuberculosis* [1]. Extracts of the litter from this tree inhibit *Staph. aureus* [2]. See [1] Gottshall et al., 1949; [2] Melin and Wikén, 1946.

Acer pseudo-platanus, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acerates viridiflora, a higher plant, extracts of which are effective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Carlson, Douglas, and Robertson, 1948.

Acetabula vulgaris, a fungus, extracts of the sporophores of which are effective *in vitro* against *Staphylococcus aureus* but not against *Escherichia coli.* See Wilkins, 1946a.

Acetobacter spp., see KOJIC ACID.

Achillea ageratifolia, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Achillea clypeolata, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Achillea filipendulina, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Achillea grandiflora, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Achillea impatiens, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Achillea magna, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Achillea millefolium, a higher plant, ether extracts of the flower and leaf of which are effective *in vitro* against *Staphylococcus aureus,* while aqueous extracts of the flower and leaf and aqueous and ether extracts of the stem are ineffective. Only aqueous extracts of the flower and aqueous and ether extracts of the leaf inhibit the spores of *Neurospora crassa.* None of these extracts is effective against *Escherichia coli* [1]. Aqueous extracts of this plant are also reported to be ineffective against *Staph. aureus* and *E. coli* [2]. Extracts of the tops of the plant are found to be slightly effective in the treatment of experimental malaria [3]. In another series of tests *in vitro* aqueous extracts showed little or no inhibition of growth against *Staph. aureus, E. coli, Erwinia carotovora,* and *Phytomonas tumefaciens* [4]. See [1] Schnell and Thayer, 1949; [2] Osborn, 1943; [3] Spencer et al., 1947; [4] Hayes, 1947.

Achillea ptarmica, a higher plant, aqueous extracts of the flower and stem of which are effective *in vitro* against *Escherichia coli,* while aqueous extracts of the leaf and root are ineffective. None of these extracts inhibits *Staphylococcus aureus* or the spores of *Neurospora crassa* [1]. Aqueous extracts of this plant are also reported to be ineffective against *Staph. aureus* and *E. coli* [2]. See [1] Schnell and Thayer, 1949; [2] Osborn, 1943.

Achillea serbica, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Achimenes haageana, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Achimenes rosea, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Achorion gallinae, as test organism *in vitro,* see ASPERGILLIC ACID; CHEIROLINE; CLAVACIN; FUMIGACIN; GLIOTOXIN; MYCOPHENOLIC ACID; PENICILLIN; PROACTINOMYCIN.

Achorion gypseum, as test organism *in vitro,* see ASPERGILLIC ACID; CHEIROLINE; CLAVACIN; FUMIGACIN; GLIOTOXIN; LYCOPERSICUM PIMPINELLIFOLIUM; MYCOPHENOLIC ACID; PENICILLIC ACID; PENICILLIN; PROACTINOMYCIN; SOLANINE.

Achorion quinckeanum, as test organism *in vitro,* see ASPERGILLIC ACID; CHEIROLINE; CLAVACIN; FUMIGACIN; GLIOTOXIN; MYCOPHENOLIC ACID; PENICILLIC ACID; PENICILLIN; PROACTINOMYCIN.

Achorion schoenleinii, a fungus which causes little or no inhibition *in vitro* of *Staphylococcus aureus* and *Escherichia coli.* See Robbins et al., 1945. As test organism *in vitro,* see LYCOPERSICUM PIMPINELLIFOLIUM; MYCOSUBTILIN; SOLANINE.

Achorion violaceum, as test organism *in vitro,* see ASPERGILLIC ACID; CHEIROLINE; CLAVACIN; FUMIGACIN; GLIOTOXIN; MYCOPHENOLIC ACID; PENICILLIN; PROACTINOMYCIN.

Achras sapota, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli* [1]. Other extracts are ineffective against *Staph. aureus, E. coli,* and *Proteus* X-19 [2]. See [1] Osborn, 1943; [2] Cardoso and Santos, 1948.

Achromobacter sp., a microorganism effective *in vitro* against *Fusarium* and *Sclerotinia.* See Chudiakov, 1935.

Achromobacter spp., as test organisms *in vitro,* see ANTIBIOTIC EI5.

Achromobacter lacticum, as test organism *in vitro,* see LEPTOTAENIA DISSECTA; RHUS HIRTA.

Achromobacter stutzeri, as test organism *in vitro,* see ACTINOMYCIN.

Achyrocline flaccida, a higher plant, extracts of which are ineffective against experimental malaria. See Spencer et al., 1947.

Achyrocline satureioides, a higher plant, extracts of which are ineffective against experimental malaria. See Spencer et al., 1947.

Acia stenodon, a fungus, extracts of the sporophores of which are effective *in vitro* against *Staphylococcus aureus* but not against *Escherichia coli* and *Pseudomonas aeruginosa.* See Wilkins and Harris, 1944d.

Acia uda, a fungus, extracts of the sporophores of which are ineffective *in vitro* against *Staphylococcus aureus, Escherichia coli,* and *Pseudomonas aeruginosa.* See Wilkins and Harris, 1944d.

Acladium sp., as test organism *in vitro,* see ANTIBIOTIC EI5.

Acmadenia frankliniae, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli* See Osborn, 1943.

Aconitum cammarum, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

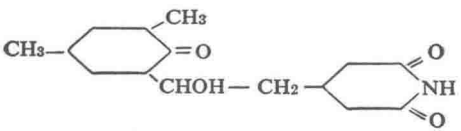
Aconitum variegatum, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Aconitum vulparia, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Acorus calamus, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli* [1]. In another series of tests *in vitro* aqueous extracts showed little or no inhibition against *Staph. aureus, E. coli, Erwinia carotovora,* and *Phytomonas tumefaciens* [2]. See [1] Osborn, 1943; [2] Hayes, 1947.

Acrostalagmus cinnabarinus, as test organism *in vitro,* see PEZIZA SCLEROTIORUM.

actidione, a crystalline antibiotic obtained from culture filtrates of *Streptomyces griseus* by chloroform extraction [1], or from its mycelia by acetone or ether extraction [2]. It is soluble in chloroform, ether, water, acetone, ethanol, and amyl acetate [1, 2, 3, 4] and is inactivated at rm. temp. by acetic anhydride, sodium acetate, and dilute alkali [3, 4]. It is thermostabile [1]. The crystals are colorless plates, the m.p. is 115°-116.5°; the empirical formula is $C_{15}H_{23}NO_4$; and the proposed structural formula [5, 12] is as follows:



SPECTRUM.—Actidione inhibits the following *in vitro* in concentrations of 1 mg/cc or less:

Asporomyces urae [6]
Blastomyces dermatitidis [6]
Cryptococcus neoformans [3]
Debaryomyces globosum [6]
Hansenula anomala [6]
Hansenula apiculata [6]
Hormodendrum pedrosoi [1]
Monosporium apiospermum [7]
Nematospora phaseoli [6]
Phialophora verrucosa [7]
Pichia membranaefaciens [6]
Powdery mildew [8]
Rhodotorula glutinis [6]
Rhodotorula sp. [1]
Saccharomyces carlsbergensis [6]
Saccharomyces cerevisiae [6]
Saccharomyces ellipsoideus v. *burgundy* [6]
Saccharomyces fragilis [6]
Saccharomyces pastorianus [6]
Schizosaccharomyces pombe [6]
Schwanniomyces occidentalis [6]
Sporobolomyces salmonicolor [6]
Torula utilis [6]
Torulaspora fermentati [6]

Waksman, Schatz, and Reilly [2] found the following to be inhibited *in vitro* (figures in parentheses denote inhibition units/gm of actidione): *Bacillus mycoides* (320,000), *B. subtilis* (800,000), *Mycobacterium avium* (11,000), and *Myco. phlei* (210,000).

The following results were obtained with 50 micrograms/cc in tests against various spp. of *Trichomonas* after 48 hr incubation [9].:

	No. of organisms/mm³		
	T. foetus	*T. gallinae*	*T. vaginalis*
Control	5,140	1,460	1,600
Actidione	1,490	0	10

The following organisms are unaffected *in vitro* by 1 mg/cc [6]:

Aerobacter aerogenes
Bacillus mycoides
Bacillus subtilis
Candida albicans
Coccidioides immitis
Endomyces magnusii
Escherichia coli
Geotrichum sp.
Hormodendrum compactum
Kloeckera apiculata
Mycotorula roseo-corrallina
Nocardia asteroides
Phytomonas campestris
Pityrosporum ovale
Proteus vulgaris
Pseudomonas aeruginosa
Saccharomyces lactis
Salmonella schottmuelleri
Sporotrichum schenckii
Staphylococcus aureus
Streptococcus fecalis
Streptococcus pyogenes
Trichophyton mentagrophytes
Trichophyton rubrum

There are fewer than 3,200 growth-inhibition units/gm of actidione for *Mycobacterium tuberculosis hominis* [2].

The activity of actidione is unaffected by the presence of whole blood or serum, but its assay is considerably affected by the size of the inoculum of the test organism, *Saccharomyces pastorianus* [6]. Susceptible strains of yeasts readily develop resistance to actidione [7].

A series of *in vitro* tests with actidione in concentrations varying from 0.001 mg to 0.008 mg/cc against *Cryptococcus neoformans* resulted in killing the various strains used [11].

TOXICITY.—The LD_{50} in rats is 2.7 mg/kg s.c. or 2.5 mg/kg i.v.; in cats, 4 mg/kg i.p.; in rabbits, 17 mg/kg i.v.; in guinea pigs, 60 mg/kg s.c. [4, 6]; in mice, 150 mg/kg i.v. [3, 4, 6]. Actidione killed mice given 2 mg/day (100 to 150 mg/kg) in 5 days, and mice given 1 mg/day (50 to 75 mg/kg) in 8 to 12 days, but it was tolerated without signs of toxicity when administered in doses of 0.1 and 0.2 mg/day [11].

ABSORPTION.—Actidione is rapidly absorbed after i.p. inj in rat, dog, and guinea pig, and is demonstrable in the plasma for at least 90 min [10].

EXPERIMENTAL CLINICAL RESULTS.—When administered to mice which have had inoculations of 90,000 organisms of one of the strains of *Cryptococcus neoformans,* actidione was without demonstrable effect when given in doses of 1 mg i.m. or s.c. to 4 mice, and in doses of 0.2 mg to 4 additional mice. Against another strain of cryptococcus administered to mice i.v. in an inoculation of 660,000 organisms, actidione likewise had no effect. In this instance 5 mice were put on a dosage schedule of 0.2 mg/day i.m. and i.v. and an

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additional 5 mice were given 1 mg/day. Treatment consisted of inj of the drug twice a day for 5 days and once a day for 14 days. The animals on larger doses of the drug apparently experienced cumulative toxic effects since they were sicker than the controls.

In man, actidione was used in only one patient and proved ineffective. Cultures of the spinal fluid, however, showed marked reduction in the number of cryptococci present in the fluid itself. This suggests an *in vitro* fungicidal effect providing the drug can be brought into direct contact with the infecting agent, especially since it was found that serum does not inactivate the drug [11]. See [1] Whiffen et al., 1946 [2] Waksman, Schatz, and Reilly, 1946; [3] Leach et al., 1947; [4] Leach and Ford, 1948; [5] Kornfeld and Jones, 1948; [6] Whiffen, 1948; [7] Whiffen, 1947a; [8] Tukey, 1948; [9] Waksman, Harris, Kupferberg, Singher, and Styles, 1949; [10] Goth and Robinson, 1949a; [11] Fisher, 1950; [12] Carter and Ford, 1950.

Actinidia arguta, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Actinidia chinensis, a higher plant, aqueous extracts of which are ineffective in *vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Actinobacillus lignieresi, as test organism *in vitro,* see LICHENIFORMIN.

Actinococcus cyaneus-antibioticus, see LITMOCIDIN.

Actinomeris squarrosa, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

actinomicelina, an antibiotic produced by an organism of the *Actinomyces* group. It is heat resistant and is highly inhibitory for some gram-positive bacilli and less active against gram-negative bacilli. See "A New Antibiotic" (actinomicelina), 1948.

Actinomyces, see also STREPTOMYCES.

Actinomyces sp., an actinomycete which *in vitro* inhibits the growth of *Ophiobolus graminis.* See Broadfoot, 1933a and b.

Actinomyces spp. **1** See ACTINOMYCETIN; ANTISMEGMATIS FACTOR. **2** As test organisms *in vitro,* see NISIN; SUBTILIN; COLLETOTRICHUM GLOEOSPORIOIDES.

Actinomyces A-10, see LAVENDULIN.

Actinomyces A-105, see ACTINORUBIN.

Actinomyces albicans, an actinomycete which is effective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces alboflavus, an actinomycete which is ineffective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces albosporeus, see ACTINORUBIN.

Actinomyces albus, a microorganism which inhibits *in vitro* the growth of these fungi [1]:

Anthostomella sp.
Botrytis tulipae
Cephalothecium roseum
Colletotrichum lindemuthianum
Gloeosporium affine
Gloeosporium musarum
Physalospora cydoniae
Volutella fructi
Zygorhynchus moelleri

It is ineffective *in vitro* against *Mycococcus ruber* [2]. See [1] Alexopoulos et al., 1938; [2] Krassilnikov and Koreniako, 1939. See also ACTINOMYCETIN. As test organism *in vitro,* see STREPTOTHRICIN.

Actinomyces annulatus, an actinomycete which *in vitro* strongly inhibits *Acanthorhynchus vaccinii, Sclerotinia sclerotiorum, Glomerella cingulata,* and *Botrytis cinerea*; inhibits *Phycomyces blakesleeanus, Phoma betae,* and *Alternaria solani*; and weakly inhibits *Fomes fraxinophilus.* It is ineffective against *Stereum gausapatum.* See Alexopoulos and Herrick, 1942.

Actinomyces antibioticus, see ACTINOMYCIN.

Actinomyces aromaticus, an actinomycete which is ineffective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces asteroides, as test organism *in vitro,* see BACILLUS SP., SUBTILIN.

Actinomyces aurantiacus, an actinomycete which is effective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939. As test organism *in vitro,* see AZOTOBACTER CHROOCOCCUM; AZOTOBACTER VINELANDII; BACILLUS MEGATHERIUM; BACILLUS MESENTERICUS; BACILLUS MYCOIDES; BACILLUS PRODIGIOSUS; BACILLUS PYOCYANEUS; BACILLUS SUBTILIS; BACILLUS TUMESCENS; BACTERIUM CLOVER; BACTERIUM KIDNEY BEAN; BACTERIUM LUCERNE; BACTERIUM LUPIN; BACTERIUM MELILOT; BACTERIUM PEA; BACTERIUM RADICICOLA; BACTERIUM SOY; BACTERIUM VETCH; BUTTER BACILLUS; CORYNEBACTERIUM; ESCHERICHIA COLI; MICROCOCCUS CANDICANS; MICROCOCCUS CITREUS; MICROCOCCUS FLAVUS; MICROCOCCUS LUTEUS; MICROCOCCUS LYSODEIKTICUS; MICROCOCCUS ROSEUS; MICROCOCCUS RUBER; MIST BACILLUS; MYCOBACTERIUM; MYCOBACTERIUM ALBUM; MYCOBACTERIUM BIFIDUM; MYCOBACTERIUM BREVICALE; MYCOBACTERIUM CITREUM; MYCOBACTERIUM CYANEUM; MYCOBACTERIUM DIASTATICUM; MYCOBACTERIUM FILIFORME; MYCOBACTERIUM FLAVUM; MYCOBACTERIUM GLOBIFORME; MYCOBACTERIUM GROSSBERGER; MYCOBACTERIUM HYALINIUM; MYCOBACTERIUM LUTEUM; MYCOBACTERIUM MUCOSUM; MYCOBACTERIUM NIGRUM; MYCOBACTERIUM PHLEI; MYCOBACTERIUM RABINOWITSCH; MYCOBACTERIUM RUBRUM; MYCOBACTERIUM SMEGMA; MYCOBACTERIUM TOBLER; MYCOBACTERIUM TUBERCULOSIS; MYCOCOCCUS ALBUS; MYCOCOCCUS CAPSULATUS; MYCOCOCCUS CITREUS; MYCOCOCCUS LACTIS; MYCOCOCCUS LUTEUS; MYCOCOCCUS MUCOSUS; MYCOCOCCUS RUBER; MYCOCOCCUS TETRAGENUS; PROACTINOMYCES ALBUS; PROACTINOMYCES CHROMOGENUS; PROACTINOMYCES CITREUS; PROACTINOMYCES CORALLINUS; PROACTINOMYCES DIASTATICUS; PROACTINOMYCES FLAVUS; PROACTINOMYCES LACTIS; PROACTINOMYCES RUBER; PROACTINOMYCES VIRIDIS; PROTEUS VULGARIS; PROTEUS ZENKERI; PSEUDOMONAS FLUORESCENS; RADIOBACTER; SARCINA FLAVA; SARCINA LUTEA; SARCINA RUBRA; STAPHYLOCOCCUS AUREUS.

Actinomyces aureus, an actinomycete which is effective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces bovis, as test organism *in vitro,* see PENICILLIN.

Actinomyces californicus, see ACTINORUBIN.

Actinomyces cellulosae, an actinomycete which is ineffective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces coelicolor, an actinomycete which is ineffective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces cyancus, an actinomycete which is effective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces cylindrosporus, an actinomycete which is ineffective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces cylindrosporus viridans, an actinomycete which is ineffective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces erythreus, see ACTINORUBIN.

Actinomyces erythrochromogenus, an actinomycete which is effective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces farinosus, an actinomycete which is ineffective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces flavovirens, an actinomycete which *in vitro* inhibits *Acanthorhynchus vaccinii* and weakly inhibits *Phycomyces blakesleeanus, Sclerotinia sclerotiorum, Glomerella cingulata, Phoma betae, Botrytis cinerea, Alternaria solani, Stereum gausapatum, and Fomes fraxinophilus.* See Alexopoulos and Herrick, 1942.

Actinomyces flavoviridis, an actinomycete which is ineffective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces flavus, an actinomycete which is ineffective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces fosciculus, an actinomycete which is effective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces fradii. 1 See ACTINORUBIN. **2** As test organism *in vitro,* see QUERCETIN.

Actinomyces fumosus n. sp., an antinomycete which is effective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces fuscus, an actinomycete which is ineffective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces glaucus, an actinomycete which is effective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces globisporus, an actinomycete which is ineffective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939. As test organism *in vitro,* see AZOTOBACTER CHROOCOCCUM; AZOTOBACTER VINELANDII; BACILLUS MEGATHERIUM; BACILLUS MESENTERICUS; BACILLUS MYCOIDES; BACILLUS PRODIGIOSUS; BACILLUS PYOCYANEUS; BACILLUS SUBTILIS; BACILLUS TUMESCENS; BACTERIUM CLOVER; BACTERIUM KIDNEY BEAN; BACTERIUM LUCERNE; BACTERIUM LUPIN; BACTERIUM MELILOT; BACTERIUM PEA; BACTERIUM RADICICOLA; BACTERIUM SOY; BACTERIUM VETCH; BUTTER BACILLUS; CORYNEBACTERIUM; ESCHERICHIA COLI; MICROCOCCUS CANDICANS; MICROCOCCUS CITREUS; MICROCOCCUS FLAVUS; MICROCOCCUS LUTEUS; MICROCOCCUS LYSODEIKTICUS; MICROCOCCUS ROSEUS; MICROCOCCUS RUBER; MIST BACILLUS; MYCOBACTERIUM; MYCOBACTERIUM ALBUM; MYCOBACTERIUM BIFIDUM; MYCOBACTERIUM BREVICALE; MYCOBACTERIUM CITREUM; MYCOBACTERIUM CYANEUM; MYCOBACTERIUM DIASTATICUM; MYCOBACTERIUM FILIFORME; MYCOBACTERIUM FLAVUM; MYCOBACTERIUM GLOBIFORME; MYCOBACTERIUM GROSSBERGER; MYCOBACTERIUM HYALINUM; MYCOBACTERIUM LUTEUM; MYCOBACTERIUM MUCOSUM; MYCOBACTERIUM NIGRUM; MYCOBACTERIUM PHLEI; MYCOBACTERIUM RABINOWITSCH; MYCOBACTERIUM RUBRUM; MYCOBACTERIUM SMEGMA; MYCOBACTERIUM TOBLER; MYCOBACTERIUM TUBERCULOSIS; MYCOCOCCUS ALBUS; MYCOCOCCUS CAPSULATUS; MYCOCOCCUS CITREUS; MYCOCOCCUS LACTIS; MYCOCOCCUS LUTEUS; MYCOCOCCUS MUCOSUS; MYCOCOCCUS RUBER; MYCOCOCCUS TETRAGENUS; PROACTINOMYCES ALBUS; PROACTINOMYCES CHROMOGENUS; PROACTINOMYCES CITREUS; PROACTINOMYCES CORALLINUS; PROACTINOMYCES DIASTATICUS; PROACTINOMYCES FLAVUS; PROACTINOMYCES LACTIS; PROACTINOMYCES RUBER; PROACTINOMYCES VIRIDIS; PROTEUS VULGARIS; PROTEUS ZENKERI; PSEUDOMONAS FLUORESCENS; RADIOBACTER; SARCINA FLAVA; SARCINA LUTEA; SARCINA RUBRA; STAPHYLOCOCCUS AUREUS.

Actinomyces gougeroti, an actinomycete which *in vitro* strongly inhibits *Phycomyces blakesleeanus, Acanthorhynchus vaccinii, Sclerotinia sclerotiorum; Glomerella cingulata, Phoma betae, Botrytis cinerea, Alternaria solani, Stereum gausapatum,* and *Fomes fraxinophilus.* See Alexopoulos and Herrick, 1942.

Actinomyces graminis, as test organism *in vitro,* see POLYPEPTIN.

Actinomyces griseus, an actinomycete which is effective *in vitro* against *Mycococcus ruber.* See Krassilnikov and Koreniako, 1939. As test organism *in vitro,* see AZOTOBACTER CHROOCOCCUM; AZOTOBACTER VINELANDII; BACILLUS MEGATHERIUM; BACILLUS MESENTERICUS; BACILLUS MYCOIDES; BACILLUS PRODIGIOSUS; BACILLUS PYOCYANEUS; BACILLUS SUBTILIS; BACILLUS TUMESCENS; BACTERIUM CLOVER; BACTERIUM KIDNEY BEAN; BACTERIUM LUCERNE; BACTERIUM LUPIN; BACTERIUM MELILOT; BACTERIUM PEA; BACTERIUM RADICICOLA; BACTERIUM SOY; BACTERIUM VETCH; BUTTER BACILLUS; CORYNEBACTERIUM; ESCHERICHIA COLI; MICROCOCCUS CANDICANS; MICROCOCCUS CITREUS; MICROCOCCUS FLAVUS; MICROCOCCUS GRISEUS; MICROCOCCUS LUTEUS; MICROCOCCUS LYSODEIKTICUS; MICROCOCCUS RUBER; MIST BACILLUS; MYCOBACTERIUM; MYCOBACTERIUM ALBUM; MYCOBACTERIUM BIFIDUM; MYCOBACTERIUM BREVICALE; MYCOBACTERIUM CITREUM; MYCOBACTERIUM CYANEUM; MYCOBACTERIUM DIASTATICUM; MYCOBACTERIUM FILIFORME; MYCOBACTERIUM FLAVUM; MYCOBACTERIUM GLOBIFORME; MYCOBACTERIUM GROSSBERGER; MYCOBACTERIUM HYALINUM; MYCOBACTERIUM LUTEUM; MYCOBACTERIUM MUCOSUM; MYCOBACTERIUM NIGRUM; MYCOBACTERIUM PHLEI; MYCOBACTERIUM RABINOWITSCH; MYCOBACTERIUM RUBRUM; MYCOBACTERIUM SMEGMA; MYCOBACTERIUM TOBLER; MYCOBACTERIUM TUBERCULOSIS; MYCOCOCCUS ALBUS; MYCOCOCCUS CAPSULATUS; MYCOCOCCUS CITREUS; MYCOCOCCUS LACTIS; MYCOCOCCUS LUTEUS; MYCOCOCCUS MUCOSUS; MYCOCOCCUS RUBER; MYCOCOCCUS TETRAGENUS; PROACTINOMYCES ALBUS; PROACTINOMYCES CHROMOGENES; PROACTINOMYCES CITREUS; PROACTINOMYCES CORALLINUS; PROACTINOMYCES DIASTATICUS; PROACTINOMYCES FLAVUS; PROACTINOMYCES LACTIS; PROACTINOMYCES RUBER; PROACTINOMYCES VIRIDIS; PROTEUS VULGARIS; PROTEUS ZENKERI; PSEUDOMONAS FLUORESCENS; RADIOBACTER; SARCINA FLAVA; SARCINA LUTEA; SARCINA RUBRA; STAPHYLOCOCCUS AUREUS.

Actinomyces halstedii, an actinomycete which *in vitro* strongly inhibits *Acanthorhynchus vaccinii* and *Fomes fraxinophilus;* inhibits *Botrytis cinerea* and *Stereum gausapatum;* and weakly inhibits *Sclerotinia sclerotiorum, Glomerella*

cingulata, and *Phoma betae.* It does not inhibit *Phycomyces blakesleeanus* or *Alternaria solani.* See Alexopoulos and Herrick, 1942.

Actinomyces israeli, as test organism *in vitro,* see BACITRACIN.

Actinomyces lactis, an actinomycete which is ineffective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces lavendulae. 1 See LAVENDULIN; STREPTOTHRICIN. 2 As test organism *in vitro,* see STREPTOTHRICIN.

Actinomyces longisporus albus, an actinomycete which is effective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces longisporus ruber, an actinomycete which is effective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces madurae, an antinomycete which *in vitro* strongly inhibits *Acanthorhynchus vaccinii, Sclerotinia sclerotiorum, Glomerella cingulata, Phoma betae, Botrytis cinerea, Alternaria solani, Fomes fraxinophilus,* and *Colletotrichum gloeosporioides.* It inhibits *Phycomyces blakesleeanus* and weakly inhibits *Stereum gausapatum.* See Alexopoulos and Herrick, 1942.

Actinomyces marinolimosus, a marine actinomycete which is effective *in vitro* against *Bacillus megatherium, Bacillus mycoides, Micrococcus roseus,* and *Sarcina lutea,* and ineffective against *Bacillus anthracis, Bacillus subtilis, Corynebacterium pseudodiphthericum, Mycobacterium lacticola, Proteus vulgaris, Salmonella typhimurium, Shigella paradysenteriae, Staphylococcus aureus, Staph. citreus,* and *Streptococcus fecalis.* The medium in which this organism is cultured is also active after passage through a Seitz or Mandler filter. See Rosenfeld and ZoBell, 1947.

Actinomyces melanocyclus, an actinomycete which is ineffective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces niger, an actinomycete which is ineffective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces odoratus, an actinomycete which is effective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces pelletieri, as test organism *in vitro,* see SUBTILIN.

Actinomyces roseolus, an actinomycete which is ineffective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces roseus, an actinomycete which is ineffective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939. See also SULFACTIN.

Actinomyces ruber, an actinomycete which is ineffective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces scabies, as test organism *in vitro,* see ASPERGILLIC ACID; BERBERINE; BURDOCK; CHEIROLINE; CLAVACIN; GLIOTOXIN; MYCOPHENOLIC ACID; PENICILLIC ACID; PROACTINOMYCIN; SPIRAEA; TYROTHRICIN.

Actinomyces sulphureus, an actinomycete which is ineffective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces verne, an actinomycete which is effective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces verticillatus, an actinomycete which is ineffective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces violaceus, an actinomycete which is effective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939. See also MYCETIN. As test organism *in vitro,* see AZOTOBACTER CHROOCCOCUM; AZOTOBACTER VINELANDII; BACILLUS MEGATHERIUM; BACILLUS MESENTERICUS; BACILLUS MYCOIDES; BACILLUS PRODIGIOSUS; BACILLUS PYOCYANEUS; BACILLUS SUBTILIS; BACILLUS TUMESCENS; BACTERIUM CLOVER; BACTERIUM KIDNEY BEAN; BACTERIUM LUCERNE; BACTERIUM LUPIN; BACTERIUM MELILOT; BACTERIUM PEA; BACTERIUM RADICICOLA; BACTERIUM SOY; BACTERIUM VETCH; BUTTER BACILLUS; CORYNEBACTERIUM; ESCHERICHIA COLI; MICROCOCCUS CANDICANS; MICROCOCCUS CITREUS; MICROCOCCUS FLAVUS; MICROCOCCUS LUTEUS; MICROCOCCUS LYSODEIKTICUS; MICROCOCCUS ROSEUS; MICROCOCCUS RUBER; MIST BACILLUS; MYCOBACTERIUM; MYCOBACTERIUM ALBUM; MYCOBACTERIUM BIFIDUM; MYCOBACTERIUM BREVICALE; MYCOBACTERIUM CITREUM; MYCOBACTERIUM CYANEUM; MYCOBACTERIUM DIASTATICUM; MYCOBACTERIUM FILIFORME; MYCOBACTERIUM FLAVUM; MYCOBACTERIUM GLOBIFORME; MYCOBACTERIUM GROSSBERGER; MYCOBACTERIUM HYALINUM; MYCOBACTERIUM LUTEUM; MYCOBACTERIUM MUCOSUM; MYCOBACTERIUM NIGRUM; MYCOBACTERIUM PHLEI; MYCOBACTERIUM RABINOWITSCH; MYCOBACTERIUM RUBRUM; MYCOBACTERIUM SMEGMA; MYCOBACTERIUM TOBLER; MYCOBACTERIUM TUBERCULOSIS; MYCOCOCCUS ALBUS; MYCOCOCCUS CAPSULATUS; MYCOCOCCUS CITREUS; MYCOCOCCUS LACTIS; MYCOCOCCUS LUTEUS; MYCOCOCCUS MUCOSUS; MYCOCOCCUS RUBER; MYCOCOCCUS TETRAGENUS; PROACTINOMYCES ALBUS; PROACTINOMYCES CHROMOGENUS; PROACTINOMYCES CITREUS; PROACTINOMYCES CORALLINUS; PROACTINOMYCES DIASTATICUS; PROACTINOMYCES FLAVUS; PROACTINOMYCES LACTIS; PROACTINOMYCES RUBER; PROACTINOMYCES VIRIDIS; PROTEUS VULGARIS; PROTEUS ZENKERI; PSEUDOMONAS FLUORESCENS; RADIOBACTER; SARCINA FLAVA; SARCINA LUTEA; SARCINA RUBRA; STAPHYLOCOCCUS AUREUS.

Actinomyces violaceus niger, an actinomycete which is effective *in vitro* against *Micrococcus* ruber. See Krassilnikov and Koreniako, 1939.

Actinomyces violaceus ruber, as test organism *in vitro,* see STREPTOTHRICIN.

Actinomyces viridis, an actinomycete which is ineffective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces viridis sterilis, an actinomycete which is ineffective *in vitro* against *Micrococcus ruber.* See Krassilnikov and Koreniako, 1939.

Actinomyces viridochromogenus, an actinomycete which *in vitro* inhibits *Glomerella cingulata, Phoma betae, Alternaria solani, Stereum gausapatum,* and *Fomes fraxinophilus,* but does not inhibit *Phycomyces blakesleeanus, Acanthorhynchus vaccinii, Sclerotinia sclerotiorum,* or *Botrytis cinerea* [1]. It is reported to be ineffective *in vitro* against *Micrococcus ruber* [2]. See [1] Alexopoulos and [2] Krassilnikov and Koreniako, 1939.

actinomycete, Meredith's, see MUSARIN.

actinomycetes, as test organisms *in vitro,* see COLLETOTRICHUM GLOEOSPORIOIDES.

actinomycetin, a bacteriolytic substance extracted from the culture filtrates of *Actinomyces albus* [1] and several other *A.* spp. [2]. It is probably a polypeptide enzyme. Actinomycetin lyses dead bacteria, while the producing organism is effective against some living gram-positive bacteria. It is soluble in

water, insoluble in ether and ethanol, and is precipitated by acetone, ethanol, and ammonium sulphate [1]. The activity is thermolabile, 60°-70°C. being sufficient to destroy it [2]. Actinomycetin is nontoxic or very slightly toxic to experimental animals [1]. See [1] Waksman, 1945; [2] Hoogerheide, 1944.

actinomycin, a crystalline antibiotic isolated from the culture filtrates of *Actinomyces (Streptomyces) antibioticus* [1] and other *Streptomyces* spp. [2, 3, 4]. It was formerly thought [1] that the activity occurred in two fractions, A and B, having different antimicrobial actions; investigators now believe that the activity of the so-called "actinomycin B" is due to contamination with the A fraction [3]. The antibiotic is extracted from the filtrates with ethyl ether, petroleum ether, ethanol, and chloroform [5], and purified by chromatographic adsorption and recrystallization [6]. The active vermilion-red platelets, m.p. 250°C. (decomp.) [6], are soluble in ethyl ether, ethanol [1, 5, 6], water [1, 6], carbon disulphide [5], acetone, chloroform [5, 6], benzene, hot ethyl acetate, and 10 per cent hydrochloric acid [6]; and insoluble in petroleum ether [1] and dilute aqueous acids and alkalis [6]. The mol. wt. is 768-1,000 [6]. Actinomycin is stable to light and does not lose activity when subjected to boiling for 30 min. [6]. It is most stable in neutral or slightly acid solution, but activity lost through alkalinization is restored by subsequent neutralization [5].

SPECTRUM.—The following microorganisms are inhibited *in vitro* by 0.05-0.2 mg/cc:

Aspergillus candida [5]
Aspergillus niger [5]
Azotobacter [5]
Bacillus megatherium [7]
Bacillus mesentericus [7]
Bacillus mycoides [5, 6, 7]
Bacillus subtilis [5, 6, 7]
Diplococcus pneumoniae [7]
Escherichia coli [4, 5, 6]
Flavobacterium sp. [7]
Fusarium sp. [5]
Humicola sp. [5]
Mycobacterium phlei [7]
Penicillium sp. [5]
Pseudomonas aeruginosa [5]
Rhizopus sp. [5]
Sarcina lutea [5, 6]
Staphylococcus aureus [7]
Streptococcus pyogenes [7]
Trichoderma sp. [5]
White yeast [5]

Actinomycin also inhibits the following:

Achromobacter stutzeri [1]
Actinomyces californicus [1]
Actinomyces cellulosae [1]
Azotobacter vinelandii [1]
Bacillus cereus [1]
Bacillus macerans [1]
Bacillus polymyxa [1]
Brucella abortus [1]
Clostridium welchii [1]
Cryptococcus neoformans [8]
Erwinia carotovora [1]
Gaffkya tetragena [1]
Hemophilus pertussis [1]
Mycobacterium tuberculosis [1]
Neisseria catarrhalis [1]
Pseudomonas fluorescens [1]
Shigella gallinarum [1]
Trichophyton mentagrophytes [8]

Actinomycin is bactericidal for *Br. abortus, E. coli* [1, 5], *B. subtilis* [1], and *Sarcina lutea* [5]. It also inhibits the growth of tomato roots and causes cytolysis of *Paramecium, Glaucoma,* and *Colpidium* [7].

The following organisms are not inhibited *in vitro* by actinomycin:

Aerobacter aerogenes [5].
Aspergillus clavatus [8]
Candida albicans [8]
Corynebacterium pyogenes [7]
Dematium sp. [8]
Erwinia tracheiphila [7]
Erysipelothrix rhusiopathiae [7]
Fusarium sp. [8]
Hemophilus influenzae [7]
Hemophilus suis [7]
Pasteurella pseudotuberculosis [7]
Penicillium luteum-purpurogenum [8]
Phytomonas flaccumfaciens [7]
Phytomonas phaseoli [7]
Phytomonas ricinicola [7]
Pseudomonas aeruginosa [7]
Salmonella abortivoequina [7]
Salmonella choleraesuis [7]
Salmonella schottmuelleri [7]
Serratia marcescens [7, 8]
Staphylococcus muscae [7]

TOXICITY.—Actinomycin is highly toxic; 10 micrograms/20 gm mouse is lethal i.v., i.p., and s.c. [4, 5, 6]. The lethal dose for fowl is 0.5-1.0 mg/2.5 kg [5]. The MTD in mice is 5 mk/kg p.o. and 0.15 mg/kg i.v., i.p., or s.c. [9]. See [1] Waksman and Woodruff, 1940a; [2] Welch, 1948; [3] Waksman, Geiger, and Reynolds, 1946; [4] Trussell and Richardson, 1948; [5] Waksman and Woodruff, 1941; [6] Waksman and Tishler, 1942; [7] Welsch, 1941; [8] Reilly et al, 1945; [9] Waksman, 1945.

actinomycosis, clinical, see BACITRACIN; PENICILLIN.

actinorubin, an antibiotic derived from an unidentified *Actinomyces* designated as *Actinomyces* A-105. It resembles *A. erythreus, A. fradii, A. albosporeus,* and *A. californicus.* The active material is purified by the same method used for LAVENDULIN. The assay of actinorubin is also the same as that of lavendulin. The m.p. of the helianthate derivative is 206°-214°C. (corr., decomp.) [1].

Staphylococcus aureus is inhibited *in vitro* by 0.2-0.55 micrograms/cc [2]. *Escherichia coli* also is inhibited by actinorubin [1].

TOXICITY.—Mice weighing 17-19 gm survive i.v. injs of 0.25 mg for at least 14 days; 1.37 mg causes 100 percent mortality in 5 days. Survivors of large doses fail to gain weight normally or actually lose weight. At autopsy the kidney and liver are found to be damaged and the thymus and spleen are reduced in size. In some cases there is evidence of recovery from liver damage [2].

ABSORPTION.—Intraperitoneal injection of 1.3 mg of actinorubin in mice results in detectable quantities in the blood up to 75 min post inj. No actinorubin is found in the blood as early as 15 min after administration of 3.43 mg to mice by stomach tube [2].

EXPERIMENTAL CLINICAL RESULTS.—When 17-19 gm mice are infected with 1 cc of a 10^{-6} dilution of *Klebsiella pneumoniae,* i.v. inj of 13.7 micrograms gives complete protection, and injection of 3.4 micrograms gives 60

percent protection. With an infecting inoculum of 1 cc of a 10^{-5} dilution of *Klebsiella pneumoniae*, i.v. inj of 30 micrograms protects 50 percent of the experimental mice, while inj of 2.5-5.0 micrograms is almost entirely ineffective [2]. See [1] Junowicz-Kocholaty and Kocholaty, 1947; [2] Morton, 1947a.

Adansonia digitata, a higher plant, extracts of which are ineffective against experimental malaria. See Spencer et al., 1947.

Adenia obtusa, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli*. See Osborn, 1943.

Adenocalymna nitidum, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli*. See Osborn, 1943.

Adenocarpus anagyrus, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli*. See Osborn, 1943.

Adenostoma sparsifolium, a higher plant, extracts of which are ineffective against experimental malaria. See Spencer et al., 1947.

Adhatoda cydoniaefolia, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli*. See Osborn, 1943.

Adhatoda vasica, a higher plant, extracts of which are ineffective against experimental malaria. See Spencer et al., 1947.

Adiantum pedatum, a higher plant, extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli* [1]. In another series of tests *in vitro* aqueous extracts showed little or no inhibition of growth against *Staph. aureus, E. coli, Erwinia carotovora,* and *Phytomonas tumefaciens* [2]. See [1] Schnell and Thayer, 1949; [2] Hayes, 1947.

Adonis autumnalis, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli*. See Osborn, 1943.

Adonis vernalis, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli*. See Osborn, 1943.

Adoxa moschatellina, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli*. See Osborn, 1943.

Aegle sepiaria, a higher plant, aqueous extracts of which are effective *in vitro* against *Staphylococcus aureus* but not against *Escherichia coli*. See Osborn, 1943.

Aegopodium podagraria, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli*. See Osborn, 1943.

Aerobacter spp., as test organisms *in vitro,* see POLYMYXINS; STREPTOMYCIN.

Aerobacter aerogenes. **1** As test organism *in vitro,* see ACTIDIONE; ACTINOMYCIN; ALLICIN; ANTIBIOTIC 136; ANTIBIOTIC 3510; ANTIBIOTIC EI_5; ANTIBIOTIC XG; ASPERGILLIC ACID; ASPERGILLIN; AUREOMYCIN; BACILLUS sp.; BACILLUS LARVAE; BACITRACIN; BIOCERIN; CENTAUREA MACULOSA; CHAETOMIN; CHLORAMPHENICOL; CLAVACIN; FUMIGACIN; GLIOTOXIN; GRISEIN; HIRSUTIC ACIDS; KOJIC ACID; LEPTOTAENIA MULTIFEDA; LUPULON AND HUMULON; NEOMYCIN; NOCARDIA GARDNERI; PERSOONIA PINIFOLIUS; POLYMYXINS; PSALLIOTA XANTHODERMA; PSEUDOMONAS FLUORESCENS; PTERYGOSPERMIN; PUCHIIN; QUERCETIN; STREPTOLIN; STREPTOMYCES ANTIBIOTICUS; STREPTOMYCES AUREOFACIENS; STREPTOMYCES GRISEUS; STREPTOMYCES LAVENDULAE; STREPTOMYCES VENEZUELAE; STREPTOTHRICIN; SUBTENOLIN; SUBTILIN; SULFACTIN; TERRAMYCIN; TRICHOPHYTON MENTAGROPHYTES; TRICHOPHYTON TONSURANS; TRICHOPHYTON VIOLACEUM; XANTHOMYCINS A AND B. For literature, see Burkholder and Evans, 1945 (lichens); Burkholder et al., 1944 (lichens); Cook and Lacey, 1945b (fungi). **2** Effect of endotoxin in mice, see PENICILLIN. **3** Treatment of urinary infections, clinical, caused by, see AUREOMYCIN; STREPTOMYCIN.

Aerobacter cloacae, as test organism *in vitro,* see BACITRACIN.

Aerobacter polymyxa, as test organism *in vitro,* see STREPTOLIN.

Aerosporin, see POLYMYXINS.

Aeschynanthus javanica, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli*. See Osborn, 1943.

Aesculus carnea, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli*. See Osborn, 1943.

Aesculus hippocastanum, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli* [1]. In another series of tests *in vitro* aqueous extracts showed little or no inhibition of growth against *Staph. aureus, E. coli, Erwinia carotovora,* and *Phytomonas tumefaciens* [2]. [1] Osborn, 1943; [2] Hayes, 1947.

Aesculus parviflora, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli*. See Osborn, 1943.

Aethionema pulchellum, a higher plant, aqueous extracts of which are effective *in vitro* against *Staphylococcus aureus* but not against *Escherichia coli*. See Osborn, 1943.

Aextoxicon punctatum, a higher plant, aqueous extracts of which are effective *in vitro* against *Staphylococcus aureus* but not against *Escherichia coli*. See Osborn, 1943.

Aframomum melagheta, a higher plant, extracts of which are ineffective against experimental malaria. See Spencer et al., 1947.

Afrormosia laxiflora, a higher plant, extracts of the roots of which are slightly effective in the treatment of experimental malaria. See Spencer et al., 1947.

Agalinis purpurea, a higher plant, extracts of the flower, stem, and leaf, but not of the roots, of which are effective *in vitro* against *Staphylococcus aureus*. Only extracts of the stem and leaf inhibit *Escherichia coli,* and none of these extracts inhibits the spores of *Neurospora crassa*. See Schnell and Thayer, 1949.

Agapetes buxifolia, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli*. See Osborn, 1943.

Agapetes mannii, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli*. See Osborn, 1943.

Agastache nepetoides, a higher plant, extracts of the leaves of which are effective *in vitro* against *Staphylococcus aureus* but not against *Escherichia coli*. Extracts of the seeds inhibit *E. coli* but not *Staph. aureus*. See Carlson, Douglas, and Robertson, 1948.

Agave sp., a higher plant, extracts of which are ineffective against experimental malaria. See Spencer et al., 1947.

Agave americana, a higher plant, extracts of which are ineffective *in vitro* against *Staphylococcus aureus, Escherichia coli,* and *Proteus* X-19. See Cardoso and Santos, 1948.

Agave attenuata, a higher plant, extracts of which are ineffective *in vitro* against *Staphylococcus aureus, Escherichia coli,* and *Mycobacterium tuberculosis.* See Gottshall et al., 1949.

Ageratum houstonianum, a higher plant, extracts of the root but not of the flower, stem, and leaf of which are effective *in vitro* against the spores of *Neurospora crassa.* None of these extracts is effective against *Staphylococcus aureus* and *Escherichia coli* [1]. Aqueous extracts of this plant are also reported to be ineffective against *Staph. aureus* and *E. coli* [2]. See [1] Schnell and Thayer, 1949; [2] Osborn, 1943.

Aglaia odorata, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Aglaonema pictum, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Agonis flexuosa, a higher plant, aqueous extracts of which are effective *in vitro* against *Staphylococcus aureus* but not against *Escherichia coli.* See Osborn, 1943.

Agonis linearifolia, a higher plant, extracts of which are effective *in vitro* against *Staphylococcus aureus* but not against *Salmonella typhi* [1, 2]. See [1] Atkinson and Rainsford, 1949; [2] Atkinson, 1949.

agranulocytosis, clinical, see PENICILLIN.

Agrimonia sp., a higher plant, aqueous extracts of which show little or no inhibition of growth when tested *in vitro* against *Staphylococcus aureus, Escherichia coli, Erwinia carotovora,* and *Phytomonas tumefaciens.* See Hayes, 1947.

Agrimonia eupatoria, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Agrimonia parviflora, a higher plant, extracts of which are ineffective *in vitro* against *Bacillus subtilis* and *Escherichia coli.* See Sanders et al., 1945.

Agrimonia striata, a higher plant, extracts of which are effective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Carlson, Douglas, and Robertson, 1948.

Agrobacterium spp., as test organisms *in vitro,* see LEPTOTAENIA DISSECTA; RHUS HIRTA.

Agrobacterium tumefaciens, as test organism *in vitro* see STREPTOMYCES VENEZUELAE; CHLORAMPHENICOL.

Agrocybe dura, a fungus which is effective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* Against *Staphylococcus aureus* culture media are effective *in vitro* at 1:512. See Hervey, 1947.

Agrocybe semiorbicularis, a fungus which is effective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Hervey, 1947.

Agropyrum repens, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Agrostemma githago, a higher plant, aqueous extracts of which show little or no inhibition of growth when tested *in vitro* against *Staphylococcus aureus, Escherichia coli, Erwinia carotovora,* and *Phytomonas tumefaciens.* See Hayes, 1947.

Ailanthus altissima, a higher plant, extracts of which are ineffective *in vitro* against *Bacillus subtilis* and *Escherichia coli.* See Sanders et al., 1945.

Ailanthus excelsa, a higher plant, extracts of which are ineffective against experimental malaria. See Spencer et al., 1947.

Ailanthus glandulosa, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli* [1]. Extracts of the wood are slightly effective against experimental malaria [2]. See [1] Osborn, 1943; [2] Spencer et al., 1947.

Ailanthus imberbiflora, a higher plant, extracts of the bark of which are effective in the treatment of experimental malaria. See Spencer et al., 1947.

Aira caespitosa, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Ajuga chamaepitys, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Ajuga iva, a higher plant, extracts of which are slightly effective in the treatment of experimental malaria. See Spencer et al., 1947.

Ajuga reptens, a higher plant, various extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli* [1] and *in vivo* against experimental malaria [2]. See [1] Osborn, 1943; [2] Spencer et al., 1947.

Akebia quinata, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Alberta magna, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

Alcaligenes spp., as test organisms *in vitro,* see AUREOMYCIN.

Alcaligenes fecalis. 1 as test organism *in vitro,* see ANTISMEGMATIS FACTOR; BACILLUS VULGATUS; BACITRACIN; CENTAUREA MACULOSA; CHLORAMPHENICOL; EPIDERMOPHYTON FLOCCOSUM; KOJIC ACID; LUPULON AND HUMULON; MYCOSUBTILIN; NOCARDIA GARDNERI; ONCOPELTUS FASCIATUS; PROTOANEMONIN; STREPTOMYCES ANTIBIOTICUS; STREPTOMYCES GRISEUS; STREPTOMYCES LAVENDULAE; STREPTOMYCES VENEZUELAE; SUBTILIN; SULFACTIN; THUJA PLICATA; TRICHOPHYTON MENTAGROPHYTES; TRICHOPHYTON TONSURANS; TRICHOPHYTON VIOLACEUM. For literature see Burkholder and Evans, 1945 (lichens); Burkholder et al., 1944 (lichens). **2** Treatment of urinary infections, clinical, caused by, see STREPTOMYCIN.

Alcaligenes metalcaligenes, as test organism *in vitro,* see CHLORAMPHENICOL.

Alcaligenes viscosus, as test organism *in vitro,* see ANTIBIOTIC 136, LUPULON AND HUMULON; SUBTILIN; XANTHOMYCINS A AND B.

Alchemilla arvensis, a higher plant, aqueous extracts of which are ineffective *in vitro* against *Staphylococcus aureus* and *Escherichia coli.* See Osborn, 1943.

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