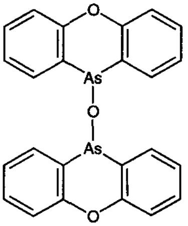
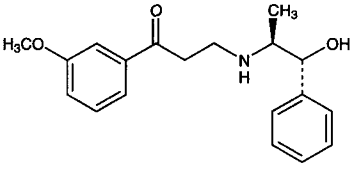
bactericide in plastics: C. C. Yeager, **US 3288674** (1966 to Scientific Chemicals). Toxicity study: D. G. Clark, *Toxicol. Appl. Pharmacol.* **21,** 315 (1972).



Colorless monoclinic prisms, mp 184-185°. dec. 380°. sp. gr. 1.40-1.42. Sol in alcohol, chloroform, methylene chloride. Practically insol in water (5 ppm at 20°) and alkali. LD_{50} in male rats: 35-50 mg/kg (Ventron, company data sheet).

USE: Primarily for fungicidal and bactericidal protection of plastics.

6962. Oxyfedrine. [15687-41-9] 3-[[(1*S*,2*R*)-2-Hydroxy-1-methyl-2-phenylethyl]amino]-1-(3-methoxyphenyl)-1-propanone; L-3-[(β-hydroxy-α-methylphenethyl)amino]-3′-methoxypropiophenone; L-(1-hydroxy-1-phenyl-2-propylamino)-1-(*m*-methoxyphenyl)-1-propanone; oxyphedrine. $C_{19}H_{23}NO_3$; mol wt 313.39. C 72.82%, H 7.40%, N 4.47%, O 15.32%. Partial β-adrenergic agonist with coronary vasodilating and positive inotropic effects. Prepn: K. Thiele, **BE 630296**; *idem,* **US 3225095** (1963, 1965 both to Degussa). K. Thiele *et al., Arzneim.-Forsch.* **16,** 1064 (1966). Absolute configuration determined by circular dichroism: J. Engel *et al., Chem. Ztg.* **105,** 85 (1981). TLC determn: Musumarra, *J. Chromatogr.* **350,** 151 (1985). Pharmacology: H. Hueller *et al., Pharmazie* **27,** 242 (1972). Mode of action: P. Mentz, W. Forster, *Arzneim.-Forsch.* **34,** 1739 (1984); N. Sternitzke, *Z. Kardiol.* **73,** 586 (1984). In prevention of experimental myocardial necrosis in rats: S. D. Seth *et al., Arzneim.-Forsch.* **34,** 678 (1984). Comparison with atenolol, *q.v.,* in angina pectoris: L. Fananapazir, C. Bray, *Br. J. Clin. Pharmacol.* **20,** 405 (1985).

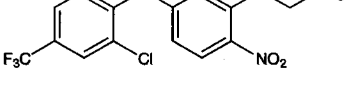


L-Form hydrochloride. [16777-42-7] D-563; Ildamen; Modacor. $C_{19}H_{23}NO_3.HCl$; mol wt 349.85. Crystals from methanol, mp 192-194°. LD_{50} in mice (mg/kg): 29 i.v. (Hueller).

DL-Form hydrochloride. [16648-69-4] mp 173-175°. LD_{50} in mice (mg/kg): 34 i.v. (Hueller).

THERAP CAT: Antianginal. Treatment of coronary insufficiency.

6963. Oxyfluorfen. [42874-03-3] 2-Chloro-1-(3-ethoxy-4-nitrophenoxy)-4-(trifluoromethyl)benzene; 2-chloro-α,α,α-trifluoro-*p*-tolyl-3-ethoxy-4-nitrophenyl ether; RH-2915; Delta Goal; Goal. $C_{15}H_{11}ClF_3NO_4$; mol wt 361.70. C 49.81%, H 3.07%, Cl 9.80%, F 15.76%, N 3.87%, O 17.69%. Selective pre- and post-emergence herbicide. Prepn: **NL 7303590**; H. O. Bayer *et al.,* **US 3798276** (1973, 1974 both to Rohm & Haas). Activity: R. Y. Yih, C. Swithenbank, *J. Agric. Food Chem.* **23,** 592 (1975). Metabolism: I. L. Adler *et al., ibid.* **25,** 1339 (1977).



Orange crystalline solid, mp 83-84°. Soly in water: 0.1 ppm. Sol in most organic solvents. LD_{50} orally in male albino rats: >5000 mg/kg (Yih, Swithenbank).

USE: Herbicide.

6964. Oxygen. [7782-44-7] O; at. wt 15.9994; at. no. 8; valence 2. Group VIA (16). Occurs normally as the diatomic gas O_2, also as ozone O_3. Atomic oxygen (O) can be prepd. Three naturally occurring isotopes: 16 (99.759%); 17 (0.037%); 18 (0.204%); artificial radioactive isotopes: 13-15; 19; 20. The most abundant element on earth; makes up 46.6% of earth's crust; 20.95% by vol of dry air. Obtained on a large scale by liquefaction of air. First obtained by Scheele in 1771 and independently by Priestley in 1774. Monograph: M. Ardon, *Oxygen: Elementary Forms and Hydrogen Peroxide* (Benjamin, New York, 1965) 106 pp. Review of oxygen and its compounds: Ebsworth *et al.,* in *Comprehensive Inorganic Chemistry* **vol. 2,** J. C. Bailar, Jr. *et al.,* Eds. (Pergamon Press, Oxford, 1973) pp 685-794; A. H. Taylor in *Kirk-Othmer Encyclopedia of Chemical Technology* **vol. 16** (Wiley-Interscience, New York, 3rd ed., 1981) pp 653-673.

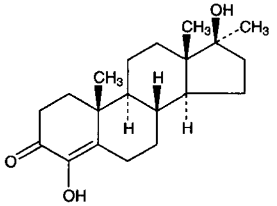
Colorless, odorless, tasteless, neutral gas; supports combustion. d^0 (gas) 1.429 g/l; d^{-183} (liquid) 1.14 g/ml. mp −218.4°. bp −182.96°. Critical temp −118.95°. Critical press. 50.14 atm. Heat of vaporization (−183°): 50.9 cal/g. Usually marketed under pressure in metal cylinders. One vol gas dissolves in 32 vols water at 20°; in 7 vols alcohol at 20°; also sol in other organic liquids and usually to a greater extent than in water. *Caution:* Avoid smoking, flames, electric sparks; explosion hazard.

USE: In oxyhydrogen or oxyacetylene flame for welding metals and for lighting (calcium light, etc); submarine work by divers, propellant for rockets. In the production of synthesis gas which can be used in the Fischer-Tropsch process for liquid fuels.

THERAP CAT: Medicinal gas to relieve hypoxia; at hyperbaric pressures in cardiac and other surgery, anaerobic infections, carbon monoxide poisoning; in cryotherapy (liq form).

THERAP CAT (VET): In hypoxia and in conjunction with volatile anesthetics.

6965. Oxymesterone. [145-12-0] (17β)-4,17-Dihydroxy-17-methylandrost-4-en-3-one; 4,17β-dihydroxy-17α-methyl-3-oxo-androst-4-ene; 4-hydroxy-17α-methyltestosterone; 17α-methyl-4-androstene-4,17β-diol-3-one; oxymestrone; Anamidol; Oranabol; Theranabol. $C_{20}H_{30}O_3$; mol wt 318.45. C 75.43%, H 9.50%, O 15.07%. Prepn: **GB 848288**; Camerino *et al.,* **US 3060201** (1960, 1962 to Farmitalia).

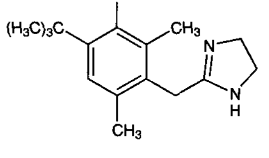


Crystals, mp 169-171°. $[\alpha]_D^{20}$ +69° (ethanol). uv max (ethanol): 278 nm ($E_{1cm}^{1\%}$ 406). Practically insol in water. Sol in chloroform, acetone, alcohol.

Note: This is a controlled substance (anabolic steroid): **21 CFR,** 1308.13, as defined in 1300.01.

THERAP CAT: Androgen; anabolic.

6966. Oxymetazoline. [1491-59-4] 3-[(4,5-Dihydro-1*H*-imidazol-2-yl)methyl]-6-(1,1-dimethylethyl)-2,4-dimethylphenol; 6-*tert*-butyl-3-(2-imidazolin-2-ylmethyl)-2,4-dimethylphenol; 2-(4-*tert*-butyl-2,6-dimethyl-3-hydroxybenzyl)-2-imidazoline; H-990; Navisin; Hazol; Rhinofrenol; Rhinolitan; Sinerol; Nezeril. $C_{16}H_{24}N_2O$; mol wt 260.37. C 73.81%, H 9.29%, N 10.76%, O 6.14%. Prepd from (4-*tert*-butyl-2,6-dimethyl-3-hydroxyphenyl)acetonitrile and ethylenediamine: Fruhstorfer, Mueller-Calgan, **DE 1117588** (1961 to E. Merck), *C.A.* **57,** 4674a (1962). Toxicity data: Hotovy *et al., Arzneim.-Forsch.* **11,** 1016 (1961).



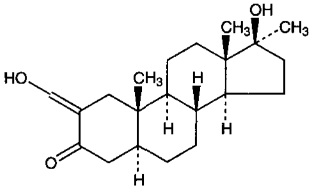
Crystals from benzene, mp 181-183°.

Hydrochloride. [2315-02-8] Afrazine; Afrin; Iliadin; Nafrine; Nasivin; Oxilin; Sinex. $C_{16}H_{24}N_2O.HCl$; mol wt 296.84. Crystals, dec 300-303°. Freely sol in water, alcohol. Practically insol in ether, chloroform, benzene. LD_{50} orally in mice: 10 mg/kg (Hotovy).

Note: Ingredient of ***Drixin***.

THERAP CAT: Adrenergic (vasoconstrictor); nasal decongestant.

6967. Oxymetholone. [434-07-1] (5α,17β)-17-Hydroxy-2-(hydroxymethylene)-17-methylandrostan-3-one; 2-hydroxymethylene-17α-methyldihydrotestosterone; 4,5α-dihydro-2-hydroxymethylene-17α-methyltestosterone; 2-hydroxymethylene-17α-methyl-17β-hydroxy-5α-androstan-3-one; 2-hydroxymethylene-17α-methylandrostan-17β-ol-3-one; anasterone; Adroyd; Anapolon; Anadrol; Pardroyd; Plenastril; Protanabol; Nastenon; Synasteron. $C_{21}H_{32}O_3$; mol wt 332.48. C 75.86%, H 9.70%, O 14.44%. Anabolic steroid. Prepn: Ringold *et al., J. Am. Chem. Soc.* **81,** 427 (1959); Ringold, Rosenkranz, **DE 1070632** (1959 to Syntex).



Crystals from ethyl acetate, mp 178-180°. $[\alpha]_D$ +38°. uv max: 285 nm (log ε 3.99).

Enol acetate. $C_{23}H_{34}O_4$. Crystals from hexane, mp 144-148°. $[\alpha]_D$ +27° (ethanol). uv max: 255 nm (log ε 4.09).

Enol propionate. $C_{24}H_{36}O_4$. Crystals from hexane, mp 135°. $[\alpha]_D$ +26° (ethanol). uv max: 257 nm (log ε 4.11).

Enol benzoate. $C_{28}H_{36}O_4$. Crystals from acetone + water, mp 188-190°. uv max: 230 nm (log ε 4.19).

Caution: Oxymetholone is reasonably anticipated to be a human carcinogen: *Report on Carcinogens, Eleventh Edition* (PB2005-104914, 2004) p III-211. This is a controlled substance (anabolic steroid): **21 CFR,** 1308.13, as defined in 1300.01.

THERAP CAT: Androgen.

THERAP CAT (VET): Anabolic steroid for small animals.

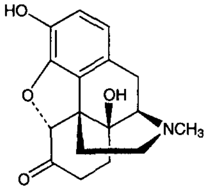
6968. Oxymethurea. [140-95-4] *N,N'*-Bis(hydroxymethyl)urea; *N,N'*-dihydroxymethylurea; Methural. $C_3H_8N_2O_3$; mol wt 120.11. C 30.00%, H 6.71%, N 23.32%, O 39.96%. $(HOCH_2NH)_2CO$. Prepn: Einhorn, Hamburger, *Ber.* **41,** 26 (1908); Walter, **US 1863426** (1927); **US 2436355** (1946 to du Pont).

Crystals from alcohol, mp 137-139°. Very sol in cold water, hot ethyl alcohol, methanol.

USE: In the textile industry in cotton crease- and shrink-proofing, finishing, drying, sizing; in tanning; pesticides; in photographic developers.

THERAP CAT: Antiseptic.

6969. Oxymorphone. [76-41-5] (5α)-4,5-Epoxy-3,14-dihydroxy-17-methylmorphinan-6-one; dihydrohydroxymorphinone; dihydro-14-hydroxymorphinone; 14-hydroxydihydromorphinone. $C_{17}H_{19}NO_4$; mol wt 301.34. C 67.76%, H 6.36%, N 4.65%, O 21.24%. Obtained from dihydrohydroxycodeinone by boiling with concd aq hydrobromic acid: Weiss, *J. Am. Chem. Soc.* **77,** 5891 (1955); Lewenstein, Weiss, **US 2806033** (1957).



Crystals from boiling ethanol, ethyl acetate or benzene. mp 248-249° (dec). Levorotatory. Sol in boiling acetone and chloroform; readily sol in aq alkalies; moderately sol in boiling ethanol; sparingly sol in benzene.

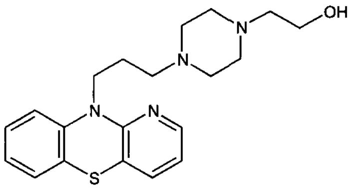
Hydrochloride. [357-07-3] Numorphan. $C_{17}H_{19}NO_4.HCl$; mol wt 337.80. Crystals.

Note: This is a controlled substance (opiate): **21 CFR,** 1308.12.

THERAP CAT: Analgesic (narcotic).

THERAP CAT (VET): Analgesic (narcotic).

6970. Oxypendyl. [5585-93-3] 4-[3-(10*H*-Pyrido[3,2-*b*][1,4]benzothiazin-10-yl)propyl]-1-piperazineethanol; 10-[3-[4-(2-hydroxyethyl)-1-piperazinyl]propyl]-10*H*-pyrido[3,2-*b*][1,4]benzothiazine; 10-[3-(1-hydroxyethyl-4-piperazinyl)propyl]-4-azaphenothiazine; oxipendyl; D-706. $C_{20}H_{26}N_4OS$; mol wt 370.51. C 64.83%, H 7.07%, N 15.12%, O 4.32%, S 8.65%. Prepn: Schuler, Klebe, *Ann.* **653,** 172 (1962).

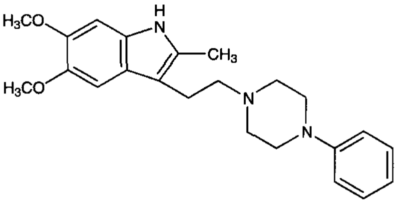


bp_1 260-265°, bp_6 280-300°.

Dihydrochloride. [17297-82-4] Pervetral. $C_{20}H_{26}N_4OS.2HCl$; mol wt 443.43. Crystals, mp 218-220°.

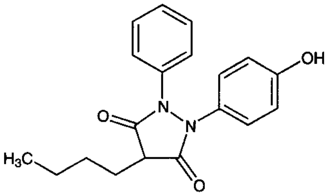
THERAP CAT: Antiemetic.

6971. Oxypertine. [153-87-7] 5,6-Dimethoxy-2-methyl-3-[2-(4-phenyl-1-piperazinyl)ethyl]-1*H*-indole; 1-[2-(5,6-dimethoxy-2-methyl-3-indolyl)ethyl]-4-phenylpiperazine; Win-18501-2; Equipertine; Forit; Integrin (formerly). $C_{23}H_{29}N_3O_2$; mol wt 379.50. C 72.79%, H 7.70%, N 11.07%, O 8.43%. Prepn: Archer *et al., J. Am. Chem. Soc.* **84,** 1306 (1962).



THERAP CAT: Antidepressant.

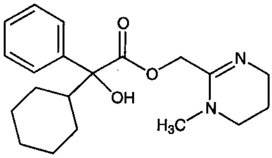
6972. Oxyphenbutazone. [129-20-4] 4-Butyl-1-(4-hydroxyphenyl)-2-phenyl-3,5-pyrazolidinedione; 4-butyl-2-(*p*-hydroxyphenyl)-1-phenyl-3,5-pyrazolidinedione; 1-phenyl-2-(*p*-hydroxyphenyl)-3,5-dioxo-4-*n*-butylpyrazolidine; 1-(*p*-hydroxyphenyl)-2-phenyl-4-butylpyrazolidine-3,5-dione; *p*-hydroxyphenylbutazone; G-27202; Californit; Crovaril; Flogitolo; Flogoril; Frabel; Neo-Farmadol; Oxalid; Rapostan; Tandearil; Visubutina. $C_{19}H_{20}N_2O_3$; mol wt 324.37. C 70.35%, H 6.21%, N 8.64%, O 14.80%. Prepn: Hafliger, **US 2745783** (1956 to Geigy); Pfister, Hafliger, *Helv. Chim. Acta* **40,** 395 (1957).



Monohydrate. [7081-38-1] Imbun; Phlogistol; Phlogase; Phlogont. Crystals, mp 96°. Anhydr crystals from ether + petr ether, mp 124-125°. Acidic reaction. Soluble in ethanol, methanol, chloroform, benzene, ether. Forms a water-soluble sodium salt.

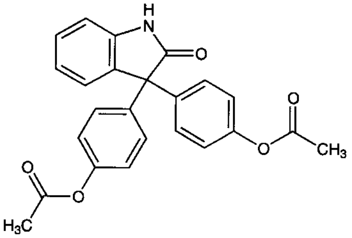
THERAP CAT: Anti-inflammatory.

6973. Oxyphencyclimine. [125-53-1] α-Cyclohexyl-α-hydroxybenzeneacetic acid (1,4,5,6-tetrahydro-1-methyl-2-pyrimidinyl)methyl ester; 1,4,5,6-tetrahydro-1-methyl-2-pyrimidinylmethyl α-phenylcyclohexaneglycolate; α-phenylcyclohexaneglycolic acid 1-methyl-2-tetrahydroxypyrimidylmethyl ester; 1-methyl-1,4,5,6-tetrahydro-2-pyrimidylmethyl α-cyclohexyl-α-phenylglycolate; Antulcus; Caridan; Daricol; Setrol; Vio-Thene; Daricon; Naridan; Zamanil. $C_{20}H_{28}N_2O_3$; mol wt 344.45. C 69.74%, H 8.19%, N 8.13%, O 13.93%. Anticholinergic. Prepn: **GB 795758** (1958 to Pfizer); Faust *et al., J. Am. Chem. Soc.* **81,** 2214 (1959).



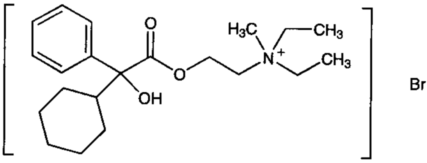
Hydrochloride. [125-52-0] $C_{20}H_{28}N_2O_3$.HCl. Crystals, dec 231-232°. Solubility in water: 1.2 g/100 ml.
THERAP CAT: Antispasmodic.

6974. Oxyphenisatin Acetate. [115-33-3] 3,3-Bis[4-(acetyloxy)phenyl]-1,3-dihydro-2*H*-indol-2-one; 3,3-bis(*p*-acetoxyphenyl)oxindole; acetphenolisatin; endophenolphthalein; diacetyldiphenolisatin; diacetyldihydroxydiphenylisatin; diacetylhydroxyphenylisatin; diacetoxydiphenylisatin; di(acetoxyphenyl)oxindole; diphesatin; diacetyldioxyphenylisatin; Isacen; Isocrin; Isaphen; Laxo-Isatin; Promassolax; Sanapert; Bydolax; Cirotyl; Lisagal; Contax; Prulet; Purgaceen; Bisatin. $C_{24}H_{19}NO_5$; mol wt 401.41. C 71.81%, H 4.77%, N 3.49%, O 19.93%. Prepd from isatin by treatment with phenol followed by acetylation in the presence of H_2SO_4 at temps below 100°: Baeyer, Lazarus, *Ber.* **18,** 2641 (1885); Hoffmann-La Roche, **CH 100806; DE 406210** (1923); **US 1624675** (1927); **DE 482435** (1929); Mizuno, Turuga, **JP 129200** (1939).



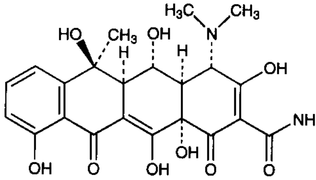
Tasteless crystals, mp 242°. Practically insol in water, ether, dilute HCl. Slightly sol in alcohol.
THERAP CAT: Cathartic.

6975. Oxyphenonium Bromide. [50-10-2] 2-[(Cyclohexylhydroxyphenylacetyl)oxy]-*N*,*N*-diethyl-*N*-methylethanaminium bromide; diethyl(2-hydroxyethyl)methylammonium α-phenylcyclohexaneglycolate bromide; α-phenylcyclohexaneglycolic acid ester diethyl(2-hydroxyethyl)methylammonium bromide; diethylaminoethyl α-phenylcyclohexaneglycolate methylbromide; 2-diethylaminoethyl α-cyclohexyl-α-phenylglycolate methobromide; cyclohexylhydroxyphenylacetic acid diethylmethylaminoethyl ester bromide; phenylcyclohexyloxyacetic acid diethylaminoethyl ester bromomethylate; Ba-5473; C-5473; Antrenyl; Spasmophen. $C_{21}H_{34}BrNO_3$; mol wt 428.40. C 58.88%, H 8.00%, Br 18.65%, N 3.27%, O 11.20%. Anticholinergic. Prepn: **CH 259948** (1949 to Ciba).



Crystals, mp 189-194° from ethyl acetate + alc. Freely sol in water. Sparingly sol in alc. Aq solns are neutral.
THERAP CAT: Antispasmodic.

6976. Oxytetracycline. [79-57-2] [4*S*-(4α,4aα,5α,5aα,6β,12aα)]-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12,12a-hexahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide; glomycin; riomitsin; hydroxytetracycline. $C_{22}H_{24}N_2O_9$; mol wt 460.43. C 57.39%, H 5.25%, N 6.08%, O 31.27%. Antibiotic substance isolated from the elaboration products of the actinomycete, *Streptomyces rimosus*, grown on a suitable medium: Finlay *et al., Science* **111,** 85 (1950). Isoln: Regna, Solomons, *Ann. N.Y. Acad. Sci.* **53,** 221 (1950); Regna *et al., J. Am. Chem. Soc.* **73,** 4211 (1951). Production from *Streptomyces rimosus:* Sobin *et al.,* **US 2516080** (1950 to Pfizer). Isoln from *S. xanthophaeus:* Brockmann, Musso, *Naturwissenschaften* **41,** 451 (1954); Brockmann *et al.,* **DE 913687** (1954 to Bayer), *C.A.* **53,** 4662h (1959). Solubility data: Weiss *et al., Antibiot. Chemother.* **7,** 374 (1957). Structure: Hochstein *et al., J. Am. Chem. Soc.* **74,** 3708 (1952). Abs config: Dobrynin *et al., Tetrahedron Lett.* **1962,** 901. Stereochemistry: Schach von Wittenau *et al., J. Am. Chem. Soc.* **87,** 134 (1965). Total synthesis of the *dl*-form: H. Muxfeldt *et al., ibid.* **101,** 689 (1979).



Stability: Oxytetracycline crystals show no loss in potency on heating for 4 days at 100°, the hydrochloride crystals show <5% inactivation after 4 mos at 56°. Aq solns of the hydrochloride at pH 1.0 to 2.5 are stable for at least 30 days at 25°. Solns at pH 3.0 to 9.0 show no detectable loss in potency on storage at 5° for at least 30 days. Half-life in hours of aq oxytetracycline solns at 37°: pH 1.0 = 114; pH 2.5 = 134; pH 4.6 = 45; pH 5.5 = 45; pH 7.0 = 26; pH 8.5 = 33; pH 10.0 = 14.

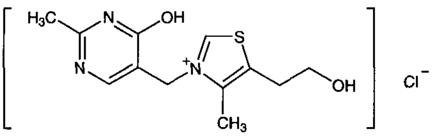
Dihydrate. Alamycin; Imperacin; Liquamycin; Terralon; Terramycin; Tetradure. Needles from water or methanol, dec 181-182°. $[\alpha]_D^{25}$ −196.6° (0.1*N* HCl); $[\alpha]_D^{25}$ −2.1° (0.1*N* NaOH); $[\alpha]_D^{25}$ +26.5° (methanol). uv max (pH 4.5 phosphate buffer 0.1*M*): 249, 276, 353 nm ($E_{1cm}^{1\%}$ 240, 322, 301). Soly in water at 23°: pH 1.2 = 31,400 μg/ml, pH 2.0 = 4600 μg/ml, pH 3.0 = 1400 μg/ml; pH 5.0 = 500 μg/ml, pH 6.0 = 700 μg/ml, pH 7.0 = 1100 μg/ml, pH 9.0 = 38,600 μg/ml. Soly in abs ethanol 12,000 μg/ml, in 95% ethanol 200 μg/ml.

Hydrochloride. [2058-46-0] Berkmycen; Duphacycline; Engemycin; Geomycin; Oxy-Mycin; Oxytetrin; Posicycline; Tetra-Tablinen; Toxinal. Yellow platelets from water. Very soluble in water (1 g/ml). Concd aq solns at neutral pH hydrolyze on standing and deposit crystals of oxytetracycline. Soly in abs ethanol: 12,000 μg/ml, in 95% ethanol: 33,000 μg/ml.

Disodium salt dihydrate. $C_{22}H_{22}N_2Na_2O_9.2H_2O$. Yellow crystals; darkens on standing. Soly in abs alc: 8,000 μg/ml, in methanol: 1500 μg/ml.
USE: To treat lethal yellowing in palm trees.
THERAP CAT: Antibacterial.
THERAP CAT (VET): Antibacterial.

6977. Oxythiamine. [582-36-5] 3-[(1,4-Dihydro-2-methyl-4-oxo-5-pyrimidinyl)methyl]-5-(2-hydroxyethyl)-4-methylthiazolium chloride; 5-(2-hydroxyethyl)-3-[(4-hydroxy-2-methyl-5-pyrimidinyl)methyl]-4-methylthiazolium chloride. $C_{12}H_{16}ClN_3O_2S$; mol wt 301.79. C 47.76%, H 5.34%, Cl 11.75%, N 13.92%, O 10.60%, S 10.62%. Prepn: F. Bergel, A. R. Todd, *J. Chem. Soc.* **1937,** 1504; M. Soodak, L. R. Cerecedo, *J. Am. Chem. Soc.* **66,** 1988 (1944). Improved prepn: H. N. Rydon, *Biochem. J.* **48,** 383 (1951). Thiamine antagonist activity: A. J. Eusebi, L. R. Cerecedo, *Science* **110,** 162 (1949); L. J. Daniel, L. C. Norris, *Proc. Soc. Exp. Biol. Med.* **72,** 165 (1949); and distribution in tissues: C. J. Gubler, D. S. Murdock, *J. Nutr. Sci. Vitaminol.* **28,** 217 (1982).

Proposed mechanism of action: S. A. Strumilo *et al.*, *Biomed. Biochim. Acta* **43,** 159 (1984). Determn by HPLC: B. C. Hemming, C. J. Gubler, *J. Liq. Chromatogr.* **3,** 1697 (1980).



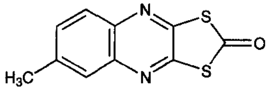
Hydrochloride. $C_{12}H_{16}ClN_3O_2S.HCl$. Flat needles grouped in rosettes, dec 195°. uv max (acid soln): 265, 258, 228, 223 nm; (alkaline soln): 268, 260, 228, 221 nm. Does not give the thiochrome reaction.

Diphosphate. Crystals, mp 127-129°.

Monophosphoric acid ester. Hygroscopic crystals, dec 185-186°.

Triphosphoric acid ester. Minute crystals, dec 245-255°.

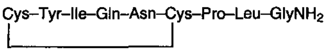
6978. Oxythioquinox. [2439-01-2] 6-Methyl-1,3-dithiolo-[4,5-*b*]quinoxalin-2-one; dithiocarbonic acid cyclic *S,S*-(6-methyl-2,3-quinoxalinediyl) ester; 6-methyl-2,3-quinoxalinedithiol cyclic *S,S*-dithiocarbonate; 6-methyl-2-oxo-1,3-dithio[4,5-*b*]quinoxaline; chinomethionat(e); quinomethionate; Bayer 36205; Forstan; Morestan. $C_{10}H_6N_2OS_2$; mol wt 234.30. C 51.26%, H 2.58%, N 11.96%, O 6.83%, S 27.37%. Prepn and review of chemical and fungicidal properties and toxicology: F. Grewe, H. Kaspers, *Pflanzenschutz-Nachr. Bayer (Engl. Ed.)* **18** (1), 1-23 (1965). Toxicity study: T. B. Gaines, *Toxicol. Appl. Pharmacol.* **14,** 515 (1969).



Yellow crystals from benzene, mp 172°. Practically insol in water. Freely sol in DMF. Sol in hot benzene, toluene, dioxane. Slightly sol in methanol, ethanol, acetone. LD_{50} in male, female rats (mg/kg): 1800, 1100 orally (Gaines).

USE: Acaricide; agricultural fungicide.

6979. Oxytocin. [50-56-6] Alpha-hypophamine; ocytocin; Intertocine-S; Perlacton; Pitocin; Syntocinon; Orasthin; Partocon; Synpitan; Uteracon. $C_{43}H_{66}N_{12}O_{12}S_2$; mol wt 1007.19. C 51.28%, H 6.60%, N 16.69%, O 19.06%, S 6.37%. The principal uterus-contracting and lactation-stimulating hormone of the posterior pituitary gland. Isoln: Pierce *et al.*, *J. Biol. Chem.* **199,** 929 (1952). Structure and synthesis: Tuppy, Michl, *Monatsh. Chem.* **84,** 1011 (1953); Tuppy, *Biochim. Biophys. Acta* **11,** 449 (1953); du Vigneaud *et al.*, *J. Am. Chem. Soc.* **75,** 4879 (1953); **76,** 3115 (1954); Bodanszky, du Vigneaud, *ibid.* **81,** 2504 (1959); Cash *et al.*, *J. Med. Pharm. Chem.* **5,** 413 (1962); Sakakibara *et al.*, *Bull. Chem. Soc. Jpn.* **38,** 120 (1965). Solid phase synthesis: Bayer, Hagenmaier, *Tetrahedron Lett.* **1968,** 2037; Ives, *Can. J. Chem.* **46,** 2318 (1968). Synthesis of D-oxytocin: Flouret, du Vigneaud, *J. Am. Chem. Soc.* **87,** 3775 (1965). Description of commercial process: Velluz *et al.*, **US 2938891** and **US 3076797** (1960, 1963, both to Roussel-UCLAF). Radioimmunoassay: T. Chard, *Clin. Biochem. Anal.* **5,** 209 (1977). *Review:* du Vigneaud, *Experientia Suppl.* **II** (14th Intl. Congr. Pure and Appl. Chem.), 9-26 (1955); R. Caldeyro-Barcia, H. Heller, *Proc. Intl. Symp. on Oxytocin* (Montevideo 1959) 443 pp; several authors, *Adv. Exp. Med. Biol.* **2,** 53-104 (1968); C. R. W. Edwards in *Hormones in Blood* **vol. 2,** C. H. Gray, V. James, Ed. (Academic Press, New York, 3rd ed., 1979) pp 401-421. Review of role in parturition: A.-R. Fuchs, F. Fuchs, *Adv. Exp. Med.* **1980,** 403-428. Comprehensive description: F. Nachtmann *et al.*, *Anal. Profiles Drug Subs.* **10,** 563-600 (1981). Book: *Oxytocin: Cellular and Molecular Approaches in Medicine and Research,* R. Ivell, J. A. Russell, Eds. (Plenum Press, New York, 1995) 673 pp.



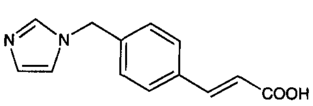
Cys–Tyr–Ile–Gln–Asn–Cys–Pro–Leu–GlyNH$_2$

White powder. $[\alpha]_D^{22}$ −26.2° (c = 0.53). Sol in water, 1-butanol, 2-butanol.

THERAP CAT: Oxytocic.

THERAP CAT (VET): Stimulates milk let-down, uterine contraction.

6980. Ozagrel. [82571-53-7] (2*E*)-3-[4-(1*H*-Imidazol-1-ylmethyl)phenyl]-2-propenoic acid; *(E)*-4-(imidazol-1-ylmethyl)-cinnamic acid; OKY-046. $C_{13}H_{12}N_2O_2$; mol wt 228.25. C 68.41%, H 5.30%, N 12.27%, O 14.02%. Prepn: K. Iizuka *et al.*, **DE 2923815**; *eidem,* **US 4226878** (both 1980 to Ono; Kissei). Synthesis and thromboxane synthetase inhibitory activity: K. Iizuka *et al.*, *J. Med. Chem.* **24,** 1139 (1981). Pharmacology: S. Hiraku *et al.*, *Jpn. J. Pharmacol.* **41,** 393 (1986). Pulmonary vascular effects: R. Garcia-Szabo *et al.*, *Prostaglandins* **28,** 851 (1984). Metabolism in animals: M. Shimizu *et al.*, *Iyakuhin Kenkyu* **17,** 289 (1986), *C.A.* **105,** 72012q (1986). HPLC determn in biological fluids: *eidem, ibid.* 298, *C.A.* **105,** 72013r (1986). Clinical pharmacology and evaluation in myocardial infarction: T. Ito *et al.*, *Biomed. Biochim. Acta* **43,** S125 (1984). Clinical evaluation in prevention of cerebral vasospasm: S. Suzuki *et al.*, *Acta Neurochir.* **77,** 133 (1985); in coronary artery disease: M. Shikano *et al.*, *Jpn. Heart J.* **28,** 663 (1987). Toxicity data: T. Nishigake *et al.*, *Clin. Rep.* **20,** 2671 (1986). Series of articles on pharmacology: *Pharmacometrics* **31,** 527-565 (1986), *C.A.* **105,** 35349-35352 (1986).



Prisms from ethanol-ether, mp 223-224°.

Hydrochloride. [78712-43-3] $C_{13}H_{12}N_2O_2.HCl$. Crystals from ethanol-ether, mp 214-217°.

Sodium salt. Cataclot; Xanbon. $C_{13}H_{11}N_2NaO_2$; mol wt 250.23. LD_{50} in male, female mice, male, female rats (mg/kg): 1940, 1580, 1150, 1300 i.v.; 3800, 3600, 5900, 5700 orally; 2450, 2100, 2300, 2250 s.c. (Nishigake).

THERAP CAT: Antithrombotic; antianginal.

6981. Ozone. [10028-15-6] Triatomic oxygen. O_3; mol wt 48.00. Found in the atm in varying proportions (about 0.05 ppm at sea level), since it is produced continuously in the outer layers of the atm by the action of solar uv radiation on the oxygen of the air. So-called sterilizing lamps operate on the same principle. In the laboratory ozone is prepd by passing dry air between two plate electrodes connected to an alternating current source of several thousand volts. The reaction is reversible, and after a little ozone has been produced it is dec at the same rate as it is generated. Obtained in pure form by cooling ozonized air to −180° when it separates as a dark blue liquid. *See also* C. E. Thorp, *Bibliography of Ozone Technology* (Armour Res. Found., Chicago). Lab prepn: *Org. Synth.* **coll. vol. III,** 673 (1955). Conference proceedings: *Adv. Chem. Ser.* **21,** entitled "Ozone Chemistry and Technology," H. A. Leedy, Ed. (ACS, Washington D.C., 1959) 465 pp. *Review:* C. Nebel in *Kirk-Othmer Encyclopedia of Chemical Technology* **vol. 16** (Wiley-Interscience, New York, 3rd ed., 1981) pp 683-713.

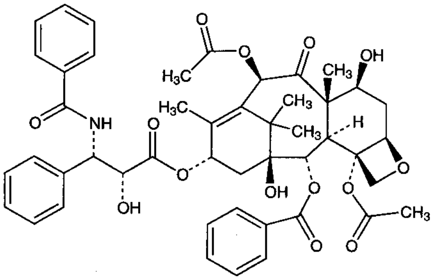
Bluish, explosive gas or blue liquid. Pleasant, characteristic odor in concns of less than 2 ppm. Irritating and injurious in higher concns. Powerful oxidizing agent. d^{0} (gas): 2.144 g/l; d$^{-195.4}$ (liq) 1.614 g/ml. mp −193°. bp −111.9°. Critical temp −12.1°. Critical press. 53.8 atm. Heat of formation 34.4 kcal/mole at 25°. Intense absorption band beginning at about 290 nm. Unstable. Solutions contg ozone explode on warming. Prepn of ozone solns in liq oxygen: Cook, **US 3008902** (1961 to Union Carbide). Although the stability of ozone in aq solns decreases as alkalinity rises, this effect is reversed at high concns. For example, the half life of ozone is 2 min in 1*N* NaOH; it is increased to 83 hrs in 20*N* NaOH: Heidt, Landi, *J. Chem. Phys.* **41,** 176 (1964).

Caution: Potential symptoms of overexposure are irritation of eyes and mucous membranes; pulmonary edema; chronic respiratory disease. *See NIOSH Pocket Guide to Chemical Hazards* (DHHS/NIOSH 97-140, 1997) p 238.

USE: As disinfectant for air and water by virtue of its oxidizing power. For bleaching waxes, textiles, oils. In organic syntheses. Forms ozonides which are sometimes useful oxidizing compds.

P

6982. Paclitaxel. [33069-62-4] (*αR,βS*)-*β*-(Benzoylamino)-*α*-hydroxybenzenepropanoic acid (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1*H*-cyclodeca[3,4]benz[1,2-*b*]oxet-9-yl ester; 5*β*,20-epoxy-1,2*α*,4,7*β*,10*β*,13*α*-hexahydroxytax-11-en-9-one 4,10-diacetate 2-benzoate 13-ester with (2*R*,3*S*)-*N*-benzoyl-3-phenylisoserine; taxol A; NSC-125973; Anzatax; Paxene; Taxol. $C_{47}H_{51}NO_{14}$; mol wt 853.91. C 66.11%, H 6.02%, N 1.64%, O 26.23%. Antiproliferative agent first isolated, as the *l*-form, from the bark of the Pacific yew tree, *Taxus brevifolia, Taxaceae;* promotes the assembly of microtubules and inhibits the tubulin disassembly process. Isoln and structure: M. C. Wani *et al., J. Am. Chem. Soc.* **93,** 2325 (1971). *In vitro* promotion of microtubule assembly: P. B. Schiff *et al., Nature* **277,** 665 (1979). Isoln from *Taxus baccala* L. and *in vitro* inhibition of depolymerization of microtubules into tubulin: G. Chauviere *et al., C.R. Seances Acad. Sci. Ser. 2* **293,** 501 (1981). Total synthesis of ***taxusin***, which contains the entire ring skeleton: R. A. Holton *et al., J. Am. Chem. Soc.* **110,** 6558 (1988). Total stereosynthesis: R. A. Holton *et al., ibid.* **116,** 1597, 1599 (1994); K. C. Nicolaou *et al., Nature* **367,** 630 (1994). Production by *Taxomyces andreanae*, an endophytic fungus associated with *T. brevifolia*: A. Stierle *et al., Science* **260,** 214 (1993). Review of mechanism of action: J. J. Manfredi, S. B. Horwitz, *Pharmacol. Ther.* **25,** 83-125 (1984); S. B. Horwitz *et al., Ann. N.Y. Acad. Sci.* **466,** 733-744 (1986); S. B. Horwitz, *Trends Pharmacol. Sci.* **13,** 134-136 (1992). Symposium on clinical toxicology, pharmacology and efficacy: *Semin. Oncol.* **20,** Suppl. 3, 1-60 (1993). Review of clinical experience in cancer therapy: T. M. Mekhail, M. Markman, *Expert. Opin. Pharmacother.* **3,** 755-766 (2002). Clinical trial in prevention of coronary artery restenosis: G. W. Stone *et al., N. Engl. J. Med.* **350,** 221 (2004).

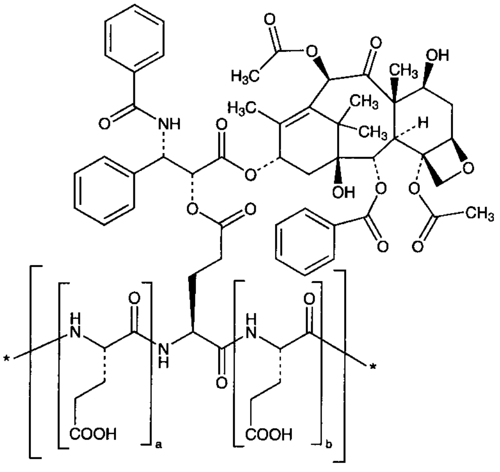


Needles from aq methanol, mp 213-216° (dec). $[\alpha]_D^{20}$ −49° (methanol). uv max (methanol): 227, 273 nm (ε 29800, 1700).

USE: Tool in study of structure and function of microtubules.

THERAP CAT: Antineoplastic; antirestenotic.

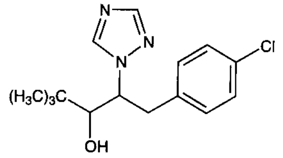
6983. Paclitaxel Poliglumex. [263351-82-2] (1*R*,2*S*)-2-(Benzoylamino)-1-[[[(2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1*H*-cyclodeca[3,4]benz[1,2-*b*]oxet-9-yl]oxy]carbonyl]-2-phenylethyl ester L-glutamic acid homopolymer; L-polyglutamic paclitaxel; PG-TXL; CT-2103; Xyotax. Biodegradable polymer drug conjugate resulting from the random condensation of L-polyglutamic acid and paclitaxel, *q.v.*, which has on average 10.4 monomeric glutamic acid units per paclitaxel-glutamate conjugate unit. Mol wt 48 kDa. Prepn: C. Li *et al., Cancer Res.* **58,** 2404 (1998). *See also*: *eidem,* **US 5977163** (1999 to PG-TXL Co.). *In vitro* activities in comparison with paclitaxel: A. S. Multani *et al., Anticancer Res.* **17,** 4269 (1997); E. A. Oldham *et al., Int. J. Oncol.* **16,** 125 (2000). Irradiation enhanced tumor specificity: C. Li *et al., Clin. Cancer Res.* **6,** 2829 (2000); L. Milas *et al., Int. J. Radiat. Oncol. Biol. Phys.* **55,** 707 (2003). Review of properties and preclinical characterization: J. W. Singer *et al., Adv. Exp. Med. Biol.* **519,** 81-99 (2003); of clinical development: J. W. Singer, *J. Controlled Rel.* **109,** 120-126 (2005); M. Man, H. Rugo, *IDrugs* **8,** 739-754 (2005).



White to off-white powder. Insol in ether; practically insol in 0.1*M* HCl and acetonitrile. Sol in 0.1*M* NaOH, 0.1*M* Na_2HPO_4 (pH 6.5); slightly sol in methanol, DMSO, dimethylformamide.

THERAP CAT: Antineoplastic.

6984. Paclobutrazol. [76738-62-0] (*αR,βR*)-*rel*-*β*-[(4-Chlorophenyl)methyl]-*α*-(1,1-dimethylethyl)-1*H*-1,2,4-triazole-1-ethanol; 1-*tert*-butyl-2-(*p*-chlorobenzyl)-2-(1,2,4-triazol-1-yl)-ethanol; (2*RS*,3*RS*)-1-(4-chlorophenyl)-4,4-dimethyl-2-(1*H*-1,2,4-triazol-1-yl)pentan-3-ol; ICI-PP-333; PP-333; Bonzi; Cultar; Parlay; Trimmit. $C_{15}H_{20}ClN_3O$; mol wt 293.79. C 61.32%, H 6.86%, Cl 12.07%, N 14.30%, O 5.45%. Plant growth regulator with fungicidal activity. Prepn: B. C. Baldwin *et al.,* **DE 2734426**; S. Balasubramanyan, M. C. Shephard, **US 4243405** (1978, 1981 both to ICI). Physical properties and biological activity: B. G. Lever *et al., Proc. Br. Crop Prot. Conf. - Weeds* **1982,** 3. Resolution and activity of isomers: B. Sugavanam, *Pestic. Sci.* **15,** 296 (1984). GC determn in plant tissue: E. A. Stahly, D. A. Buchanan, *HortScience* **21,** 534 (1986). Comparison with daminozide, *q.v.*, of effect on apple trees: G. R. Stinchcombe *et al., J. Hortic. Sci.* **59,** 323 (1984).

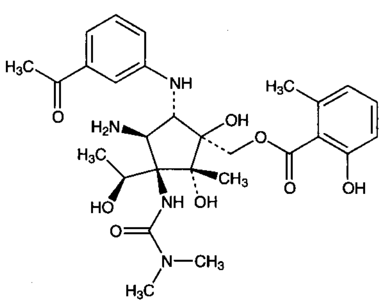


White crystalline solid, mp 165-166°. d 1.22. Vapor pressure at 20°: 1×10^{-6} Pa. Soly: water 35 mg/l, methanol 15%, propylene glycol 5%, acetone 11%, cyclohexanone 18%, methylene dichloride 10%, hexane 1%, xylene 6%.

USE: Plant growth regulator.

6985. Pactamycin. [23668-11-3] 2-Hydroxy-6-methylbenzoic acid [(1*S*,2*R*,3*R*,4*S*,5*S*)-5-[(3-acetylphenyl)amino]-4-amino-3-[[(dimethylamino)carbonyl]amino]-1,2-dihydroxy-3-[(1*S*)-1-hydroxyethyl]-2-methylcyclopentyl]methyl ester; NSC-52947; U-15800. $C_{28}H_{38}N_4O_8$; mol wt 558.62. C 60.20%, H 6.86%, N 10.03%, O 22.91%. Antitumor antibiotic produced by *Streptomyces pactum* var *pactum*. Discovery and biological properties: Bhuyan *et al., Antimicrob. Agents Chemother.* **1961,** 184. Isoln and characterization: Argoudelis *et al., ibid.* 191. Manuf: **GB 980346** (1965 to Upjohn), *C.A.* **62,** 11115f (1965). Structure: Wiley *et al., J. Org. Chem.* **35,** 1420 (1970). Revised structure: D. J. Duchamp, *Am. Crystallogr. Assn.* (Winter Mtg., Albuquerque, 1972) p 23. Mechanism of action: T. A. Beerman *et al., Adv. Enzyme Regul.* **14,** 207 (1976). ^{13}C-NMR study: D. D. Weller *et al., J. Antibiot.* **30,** 997 (1978). Biosynthesis: D. D. Weller, K. L. Rinehart, *J. Am.*

Chem. Soc. **100,** 6757 (1978). *Review:* Goldberg in *Antibiotics* **vol. 3,** J. W. Corcoran, F. E. Hahn, Eds. (Springer-Verlag, New York, 1975) pp 498-515.

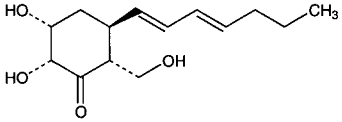


$[\alpha]_D^{25}$ +79° (ethanol) changing to +23° on standing. [α] changes in acetone on standing from +25° to +76° in 24 hours. Amphoteric. Sol in ethanol, chloroform, methylene chloride, benzene, ether, in solns <pH 5 and >9.5. Insol in Skellysolve B, cyclohexane; insol at isoelectric pt, pH 8.3. Unstable in solution. LD_{50} in mice (mg/kg): 10.7 orally; 15.6 i.v.; in rats (mg/kg): 1.4 i.v. (Bhuyan).

6986. Palifermin. [162394-19-6] 24-163-Keratinocyte growth factor (human); 24-163-fibroblast growth factor 7 (human); rHuKGF; Kepivance. Recombinant epithelial tissue growth factor of 141 amino acid residues; N-terminal truncated form of endogenous KGF. Mol wt approx 16.3 kDa. Prepn: D. J. Gospodarowicz, F. R. Masiarz, **WO 9501434**; *eidem,* **US 5677278** (1995, 1997 both to Chiron). *In vivo* radioprotective effect: C. L. Farrell *et al., Cancer Res.* **58,** 933 (1998). Clinical study in mucositis associated with myelosuppressive therapy: R. Spielberger *et al., N. Engl. J. Med.* **351,** 2590 (2004). Review of therapeutic potential in oral mucositis: M. A. A. Siddiqui, K. Wellington, *Drugs* **65,** 2139-2146 (2005); M. L. Radtke, J. M. Kolesar, *J. Oncol. Pharm. Pract.* **11,** 121-125 (2005).

THERAP CAT: Radioprotective agent.

6987. Palitantin. [15265-28-8] (2*R*,3*S*,5*R*,6*R*)-*rel*-3-(1*E*,3*E*)-1,3-Heptadienyl-5,6-dihydroxy-2-(hydroxymethyl)cyclohexanone. $C_{14}H_{22}O_4$; mol wt 254.32. C 66.12%, H 8.72%, O 25.16%. Metabolic product of *Penicillium palitans* Westling. Isoln: J. H. Birkinshaw, H. Raistrick, *Biochem. J.* **30,** 801 (1936). Derivs and degradation products: J. H. Birkinshaw, *ibid.* **51,** 271 (1952). Structure: K. Bowden *et al., J. Chem. Soc.* **1959,** 1662. Biosynthesis: P. Chaplen, R. Thomas, *Biochem. J.* **77,** 91 (1960); A. J. Birch, M. Kocor, *J. Chem. Soc.* **1960,** 866. Reactivity studies: A. T. Austin, B. Pearson, *Chem. Ind. (London)* **1966,** 1228. Stereoselective synthesis of (±)-form: A. Ichihara *et al., Tetrahedron Lett.* **1977,** 3473; *eidem, Tetrahedron* **36,** 1547 (1980).



Needles from hot water, mp 165°. $[\alpha]_{5461}^{23}$ +4.4° (c = 0.8 in $CHCl_3$). uv max (ethanol): 323 nm (ε 34,000). Sol in hot water, alc, chloroform; slightly sol in cold water, ether.

6988. Palivizumab. [188039-54-5] Anti-(respiratory syncytial virus protein F) immunoglobulin G1 (human-mouse monoclonal MEDI-493 γ_1-chain) disulfide with human-mouse monoclonal MEDI-493 κ-chain, dimer; MEDI-493; Synagis. Humanized monoclonal antibody directed to a neutralizing epitope on the F glycoprotein of respiratory syncytial virus (RSV). Mol wt ~148 kDa. Consists of ~95% human and ~5% murine antibody sequences. Prepn and neutralizing activity: L. S. Johnson, **WO 9605229**; *idem,* **US 5824307** (1996, 1998 both to MedImmune); S. Johnson *et al., J. Infect. Dis.* **176,** 1215 (1997). Clinical pharmacokinetics and safety: X. Sáez-Llorens *et al., Pediatr. Infect. Dis. J.* **17,** 787 (1998). Clinical trial in high risk infants: Impact-RSV Study Group, *Pediatrics* **103,** 531 (1998). *Review:* H. C. Meissner *et al., Pediatr. Infect. Dis. J.* **18,** 223-231 (1999).

THERAP CAT: Antiviral (in prophylaxis of RSV infection).

6989. Palladium. [7440-05-3] Pd; at. wt 106.42; at. no. 46; valences 2, 4. Group VIII (10). Six naturally occurring isotopes: 102 (1.0%); 104 (11.0%); 105 (22.2%); 106 (27.3%); 108 (26.7%); 110 (11.8%); artificial, radioactive isotopes: 98-101, 103; 107; 109; 111-115. Abundance in earth's crust 0.001-0.01 ppm. Discovered in 1803 by Wollaston. Belongs to the platinum group of metals. Occurs in nature alloyed with platinum or gold and as a selenide; found in nickel sulfide ores; found in the minerals stibiopalladinite, braggite, porpezite. Isoln: Vauguelin *et al.,* cited by Mellor, *A Comprehensive Treatise on Inorganic and Theoretical Chemistry* **15,** 595 (1936). Reviews of prepn, properties and chemistry of palladium and other platinum metals: Gilchrist, *Chem. Rev.* **32,** 277-372 (1943); Beamish *et al.,* in *Rare Metals Handbook,* C. A. Hampel, Ed. (Reinhold, New York, 1956) pp 291-328; Livingstone in *Comprehensive Inorganic Chemistry* **vol. 3,** J. C. Bailar, Jr. *et al.,* Eds. (Pergamon Press, Oxford, 1973) pp 1163-1189, 1274-1329. Review of uses: E. M. Wise, *Palladium, Recovery, Properties, Uses* (Academic Press, New York, 1968) 187 pp. Use of organic palladium derivatives in synthesis: P. M. Maitlis, *The Organic Chemistry of Palladium* (Academic Press, New York, 1971); J. Tsuji, *Top. Curr. Chem.* **91,** 29 (1980); B. M. Trost, *Tetrahedron* **33,** 2615 (1977); *idem, Acc. Chem. Res.* **13,** 385 (1980).

Silver-white metal, face-centered cubic structure; occurs also as black powder and as spongy masses which can be compressed to a compact mass. mp 1555°. bp 3167°. d_4^{20} 12.02. Hardness on Mohs' scale 4.8, Brinell hardness 61.0. Spec heat 0.0584 cal/g at 0°C. Electrical resistivity at 0° = 10.0 microohms-cm. Appreciably volatile at high temps. At a red heat is converted into the monoxide. Forms dihalides with fluorine or chlorine at a red heat. Reacts with nitric acid, sulfuric acid, a mixture of hydrochloric and chloric acids. Reacts slightly with concd HCl; more readily in the presence of air or free chlorine. Forms a sulfide when heated with sulfur, a phosphide when heated with phosphorus. Absorbs a considerable amount of hydrogen.

USE: In form of gold, silver, and copper alloys in dentistry; for alloy bearings, springs, balance wheels of watches; for mirrors in astronomical instruments; as catalyzer in manuf of sulfuric acid and in other oxidizing processes; in powder form as catalyst in hydrogenation and in ignition of hydrogen or hydrocarbons with oxygen; the spongy form is used in gas analysis for separating hydrogen from mixtures of gases.

6990. Palladium Chloride. [7647-10-1] Palladous chloride. Cl_2Pd; mol wt 177.33. Cl 39.99%, Pd 60.01%. $PdCl_2$. Prepn: Krustinsons, *Z. Elektrochem.* **44,** 537 (1938). Toxicity study: Orestano, *Boll. Soc. Ital. Biol. Sper.* **8,** 1154 (1933). Review of $PdCl_2$ and other halides: J. H. Canterford, R. Colton, *Halides of the Second and Third Row Transition Metals* (John Wiley, New York, 1968) pp 358-389.

Red crystals. mp 678-680°. Dec at high temp to palladium and chlorine. MLD i.v. in rabbits: 0.0186 g/kg (Orestano).

Dihydrate. Dark brown crystals. Sol in water, alcohol, acetone. Reduced in soln by hydrogen or CO to metal. *Keep tightly closed.*

USE: In photography, for preparing pictures to be transferred to porcelain; toning solutions; electroplating parts of clocks and watches; manuf indelible ink; for the prepn of the metal for use as a catalyst; $PdCl_2$ paper is used for detecting CO, to find leaks in buried gas pipes. Prepn of palladium catalysts using $PdCl_2$: Mozingo, *Org. Synth.* **coll. vol. III,** 685 (1955).

6991. Palladium Diacetate. [19807-27-3] Acetic acid palladium salt; bis(acetato)palladium; diacetatopalladium(II); palladium(II) acetate. $C_4H_6O_4Pd$; mol wt 224.51. C 21.40%, H 2.69%, O 28.51%, Pd 47.40%. $(CH_3COO)_2Pd$. Prepn from palladium sponge or palladium nitrate and glacial acetic acid: Morehouse *et al., Chem. Ind. (London)* **1964,** 544; Stephenson *et al., J. Chem. Soc.* **1965,** 3632; from hydrated palladium oxide and acetic acid: Hausman *et al.,* **FR 1403398** corresp to **US 3318891** (1965, 1967 to Engelhard). Crystal structure of trimeric palladium acetate: Skapski, Smart, *Chem. Commun.* **1970,** 658.

Orange-brown crystals; mp 205° (dec). Shown to be trimeric by osmometric determn of mol wt in benzene (37°); monomeric by ebullioscopic measurement in benzene (80°). Crystals are trimeric. Sol in chloroform, methylene dichloride, acetone, acetonitrile, diethyl ether; sol with dec in aq HCl, aq KI solutions. Insol in water, aq NaCl, $NaNO_3$, NaOAc solns, petroleum, alcohols. Dec when warmed with alcohols.

USE: Catalyst.

6992. Palladium Nitrate. [10102-05-3] Palladous nitrate. N_2O_6Pd; mol wt 230.43. N 12.16%, O 41.66%, Pd 46.18%. $Pd(NO_3)_2$. Prepn from palladium and nitric acid: *Gmelins, Palladium* (8th ed.) **65,** 269 (1942). Reported to be the dihydrate: Gatehouse *et al., J. Chem. Soc.* **1957,** 4222.

Brown, deliquesc crystals. Sol in water with turbidity; with much water a brown basic salt precipitates; completely sol in dil HNO_3. *Keep well closed, protected from light.*

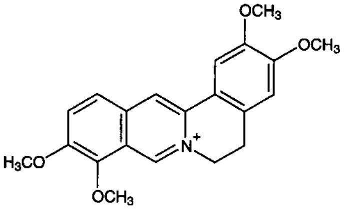
USE: Sepn of Cl_2 and I_2; catalyst in organic syntheses.

6993. Palladium Oxide. [1314-08-5] Palladium monoxide; palladous oxide. OPd; mol wt 122.42. O 13.07%, Pd 86.93%. PdO. Prepn: Shriner, Adams, *J. Am. Chem. Soc.* **46,** 1685 (1924).

Black powder. d 8.3. Insol in water, acids; slightly sol in aqua regia; sol in 48% HBr. Dec when strongly heated; also in the presence of H_2.

USE: Reduction catalyst in synthesis of organic compds.

6994. Palmatine. [3486-67-7] 5,6-Dihydro-2,3,9,10-tetramethoxydibenzo[*a,g*]quinolizinium; 7,8,13,13a-tetradehydro-2,3,9,10-tetramethoxyberbinium; calystigine. $[C_{21}H_{22}NO_4]^+$. Obtained only in form of its salts. First isolated from Calumba root *(Jateorhiza palmata* (DC.) Miers, *Menispermaceae).* Now found in many other genera. Palmatine and tetrahydropalmatine, *q.v.* are probably the most widely distributed Berberis alkaloids. Extraction procedure: Feist, Dschu, *Arch. Pharm.* **263,** 301 (1925). Structure: Feist, Sandstede, *ibid.* **256,** 2, 5 (1918); Späth, Lang, *Ber.* **54,** 3064, 3068 (1921); Späth, Böhm, *Ber.* **55,** 2988 (1922); Späth, Meinhard, *Ber.* **75,** 400 (1942). Synthesis: Späth, Quientensky, *Ber.* **58,** 2267 (1925); R. D. Haworth *et al., J. Chem. Soc.* **1927,** 548; Z. Kiparissides *et al., Can. J. Chem.* **58,** 2770 (1980). Identity with calystigine, alkaloid of the Chinese drug Chi-Kuo-Lan: Huang, Chen, *C.A.* **52,** 15827i (1958).



Palmatine forms addn products with acetone and chloroform, as does berberine.

Iodide. $(C_{21}H_{22}NO_4)I$. Yellow needles from water, dec 239°; also a dihydrate. Sparingly sol in hot water and alc.

Nitrate. $(C_{21}H_{22}NO_4)NO_3$. Sesqui- or dihydrate, yellow needles, dec 239°. Freely sol in most solvents.

Chloride trihydrate. $(C_{21}H_{22}NO_4)Cl.3H_2O$. Yellowish-green needles from water. Freely sol in hot water and alc.

Sulfate pentahydrate. $(C_{21}H_{22}NO_4)_2SO_4.5H_2O$. Yellow needles, mp 250°. Very sol in alc, sol in water.

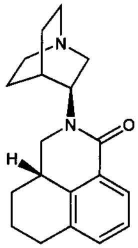
6995. Palmidrol. [544-31-0] *N*-(2-Hydroxyethyl)hexadecanamide; *N*-(2-hydroxyethyl)palmitamide. $C_{18}H_{37}NO_2$; mol wt 299.49. C 72.19%, H 12.45%, N 4.68%, O 10.68%. $CH_3(CH_2)_{14}CONHCH_2CH_2OH$. A naturally occurring anti-inflammatory agent. Isolated from soybean lecithin, egg yolk, and peanut meal: Kuehl *et al., J. Am. Chem. Soc.* **79,** 5577 (1957). Synthesis by refluxing ethanolamine with palmitic acid: Roe *et al., ibid.* **74,** 3442 (1952).

Crystals from 95% ethanol or cyclohexane, mp 98-99°.

6996. Palmitic Acid. [57-10-3] Hexadecanoic acid; hexadecylic acid; cetylic acid. $C_{16}H_{32}O_2$; mol wt 256.42. C 74.94%, H 12.58%, O 12.48%. $CH_3(CH_2)_{14}COOH$. Occurs as the glyceryl ester in many oils and fats. Obtained from palm oil, Japan wax, or Chinese vegetable tallow. Purification: Magne *et al.,* **US 2791596** (1957 to Secretary of Agriculture). Toxicity study: L. Orö, A. Wretlind, *Acta Pharmacol. Toxicol.* **18,** 141 (1961).

White, crystalline scales. d_4^{62} 0.853. mp 63-64°. bp_{15} 215°. n_D^{80} 1.4273. Insol in water. Sparingly sol in cold alcohol or in petr ether; freely sol in hot alcohol, in ether, propyl alcohol, chloroform. LD_{50} i.v. in mice: 57±3.4 mg/kg (Orö, Wretlind).

6997. Palonosetron. [135729-61-2] (3a*S*)-2-(3*S*)-1-Azabicyclo[2.2.2]oct-3-yl-2,3,3a,4,5,6-hexahydro-1*H*-benz[*de*]isoquinolin-1-one. $C_{19}H_{24}N_2O$; mol wt 296.41. C 76.99%, H 8.16%, N 9.45%, O 5.40%. Serotonin 5-HT_3 receptor antagonist. Prepn: J. Berger *et al.,* **EP 430190;** *eidem,* **US 5202333** (1991, 1993 both to Syntex); R. D. Clark *et al., J. Med. Chem.* **36,** 2645 (1993). Improved synthesis: B. A. Kowalczyk, *Heterocycles* **43,** 1439 (1996). Receptor binding study: E. H. F. Wong *et al., Br. J. Pharmacol.* **114,** 851 (1995). Pharmacology: R. M. Eglen *et al., ibid.* 860. Clinical efficacy and pharmacokinetics: P. Eisenberg *et al., Ann. Oncol.* **15,** 330 (2004). Clinical trial in prevention of chemotherapy-induced nausea and vomiting: R. Gralla *et al., Ann. Oncol.* **14,** 1570 (2003). Review of pharmacology and clinical experience: S. M. Grunberg, J. M. Koeller, *Expert. Opin. Pharmacother.* **4,** 2297-2303 (2003); M. A. A. Siddiqui, L. J. Scott, *Drugs* **64,** 1125-1132 (2004).

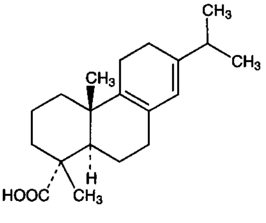


mp 87-88°. $[\alpha]_D$ −136° (c = 0.25 in chloroform).

Hydrochloride. [135729-62-3] RS-25259-197; Aloxi; Onicit. $C_{19}H_{24}N_2O.HCl$; mol wt 332.87. Crystals from ethanol, mp >290°. $[\alpha]_D^{25}$ −94.1° (c = 0.4 in water). Freely sol in water; sol in propylene glycol; slightly sol in ethanol, 2-propanol.

THERAP CAT: Antiemetic.

6998. Palustric Acid. [1945-53-5] [1*R*-(1α,4aβ,10aα)]-1,2,-3,4,4a,5,6,9,10,10a-Decahydro-1,4a-dimethyl-7-(1-methylethyl)-1-phenanthrenecarboxylic acid; 13-isopropylpodocarpa-8,13-dien-15-oic acid. $C_{20}H_{30}O_2$; mol wt 302.45. C 79.42%, H 10.00%, O 10.58%. Isoln from gum rosin: Loeblich *et al., J. Am. Chem. Soc.* **77,** 2823 (1955); Joye *et al., J. Org. Chem.* **30,** 654 (1965). Structure: Shuller *et al., J. Am. Chem. Soc.* **82,** 1734 (1960). Prepn of the 4-*epi*-form: Tabacik, Poisson, *Bull. Soc. Chim. Fr.* **1969,** 3264.

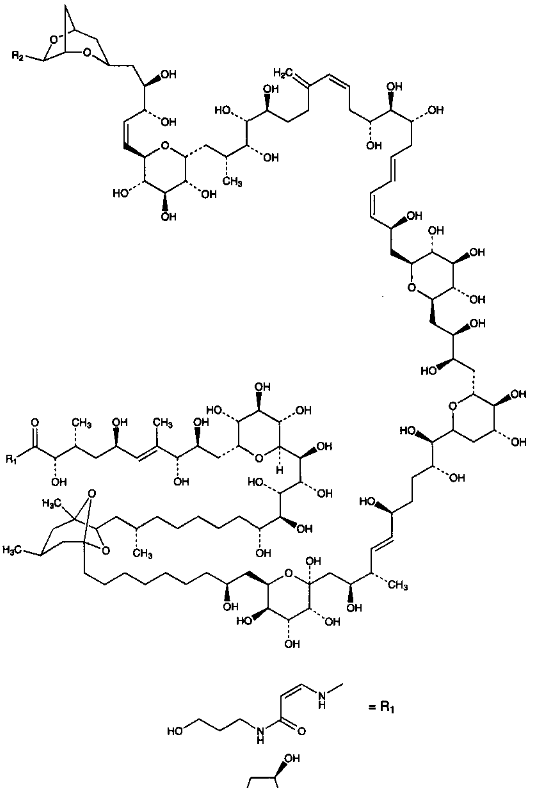


Crystals from methanol, mp 162-167°. $[\alpha]_D$ +71.6°. uv max (0.01*N* NaOH): 265-266 nm.

Methyl ester. $C_{21}H_{32}O_2$. Crystals from methanol, mp 25-27°. $[\alpha]_D$ +67.7°. uv max: 265-266 nm.

6999. Palytoxin. [77734-91-9] Palytoxin (C51-55 hemiacetal); PTX. $C_{129}H_{223}N_3O_{54}$; mol wt 2680.14. C 57.81%, H 8.39%, N 1.57%, O 32.24%. Potent toxin isolated from zoanthid coral of the genus *Palythoa* that is the most poisonous non-proteinaceous substance known. Isoln from "Limu-make-o-Hana", the Hawaiian name for the highly toxic coelenterate *Palythoa toxica:* R. E. Moore, P. J. Scheuer, *Science* **172,** 495 (1971). Structure: R. E.

Moore, G. Bartolini, *J. Am. Chem. Soc.* **103,** 2491 (1981). Structure of palytoxin from *P. tuberculosa* of Okinawa (differs from palytoxin from *P. toxica* at two positions): D. Uemura *et al., Tetrahedron Lett.* **22,** 2781 (1981). Proposed absolute configuration of 60 of the 64 chiral centers: R. E. Moore *et al., J. Am. Chem. Soc.* **104,** 3776 (1982). Structure and stereochemistry: J. K. Cha *et al., ibid.* 7369. Discussion of the structural elucidation, *see* Y. Shimizu, *Nature* **302,** 212 (1983); review: R. E. Moore, *Prog. Chem. Org. Nat. Prod.* **48,** 82-202 (1985). Synthetic studies: Y. Kishi, *Chem. Scr.* **27,** 573 (1987). Pharmacological study: P. N. Kaul *et al., Proc. West. Pharmacol. Soc.* **17,** 294 (1974). Mechanism of action and treatment of palytoxin poisoning: J. A. Vick *et al., Toxicol. Appl. Pharmacol.* **34,** 214 (1975). Mode of contractile action on vascular smooth muscle: K. Ito *et al., Eur. J. Pharmacol.* **46,** 9 (1977). Depolarizing action on frog spinal cord: Y. Kudo, S. Shibata, *Br. J. Pharmacol.* **71,** 575 (1980). Toxicology and toxicity studies: J. S. Wiles *et al., Toxicon* **12,** 427 (1974); K. Ito *et al., Arch. Int. Pharmacodyn. Ther.* **258,** 146 (1982). Brief review of biology: P. J. Scheuer, *Acc. Chem. Res.* **10,** 33-39 (1977). Review of synthetic studies and conformational analysis: Y. Kishi, *Pure Appl. Chem.* **61,** 313-324 (1989).

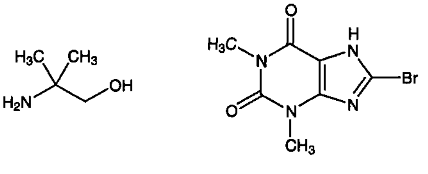


White amorphous hygroscopic solid. No definite mp; chars when heated to 300°. $[\alpha]_D^{25}$ +26° (water). Insol in chloroform, ether, acetone. Sparingly sol in methanol, ethanol. Sol in pyridine, DMSO, water. LD_{50} in mice: 0.45 μg/kg i.v. (Wiles); 50-100 ng/kg i.p. (Kaul).

Caution: Palytoxin is an intense vasoconstrictor. In intact dogs, doses of >0.06 μg/kg i.v. caused a transient rise in arterial pressure followed by rapid hypotension and resulted in death within 5 minutes (Ito, 1982).

USE: As a physiological tool to evaluate anti-anginal chemotherapeutic agents.

7000. Pamabrom. [606-04-2] 8-Bromo-3,7-dihydro-1,3-dimethyl-1*H*-purine-2,6-dione compd with 2-amino-2-methyl-1-propanol (1:1); 8-bromotheophylline compd with 2-amino-2-methyl-1-propanol (1:1); 2-amino-2-methyl-2-propanol 8-bromotheophyllinate. $C_{11}H_{18}BrN_5O_3$; mol wt 348.20. C 37.94%, H 5.21%, Br 22.95%, N 20.11%, O 13.78%. Prepn from 2-amino-2-methyl-1-propanol and 8-bromotheophylline: J. M. Holbert, I. W. Grote, **US 2711411** (1955 to Chattanooga Med.). Prepn and diuretic activity: J. M. Holbert *et al., J. Am. Pharm. Assoc. Sci. Ed.* **44,** 355 (1955).

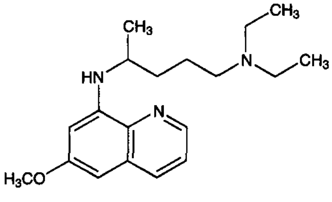


Fine white powder, dec 300°. Soly in water >30 g/100 ml at 25°. pH of satd aq soln 8.0-8.5.

Mixture with acetaminophen and pyrilamine maleate. Midol PMS; Premsyn PMS; Sunril.

THERAP CAT: Diuretic.

7001. Pamaquine. [491-92-9] N^1,N^1-Diethyl-N^4-(6-methoxy-8-quinolinyl)-1,4-pentanediamine; 8-[[4-(diethylamino)-1-methylbutyl]amino]-6-methoxyquinoline. $C_{19}H_{29}N_3O$; mol wt 315.45. C 72.34%, H 9.27%, N 13.32%, O 5.07%. Prepn: **GB 295656** (1927 to I. G. Farbenind); K. H. Slotta, *Grundriss der modernen Arzneistoff-Synthese* (Stuttgart, 1931); Elderfield *et al., J. Am. Chem. Soc.* **70,** 40 (1948). *Review:* Cooper, *Public Health Rep.* **64,** 717 (1949). HPLC determn in plasma: Y. S. Endoh *et al., J. Chromatogr.* **579,** 123 (1992). Historical review: D. Greenwood, *J. Antimicrob. Chemother.* **36,** 857-872 (1995).

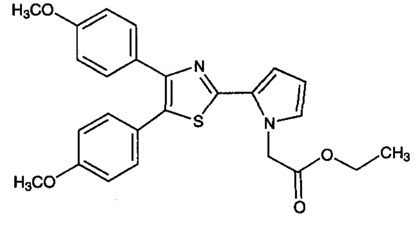


Dark yellow oil. $bp_{0.3}$ 175-180°; bp_1 182-194°.

Pamoate. [635-05-2] Pamaquine embonate; pamaquine naphthoate; Aminoquin; Plasmochin; Plasmoquine; Praequine. $C_{19}H_{29}N_3O.C_{23}H_{16}O_6$; mol wt 703.82. Yellow to orange-yellow odorless, almost tasteless powder. Numbs the tongue. Insol in water. Sol in alcohol, acetone. *Protect from light.*

THERAP CAT: Antimalarial.

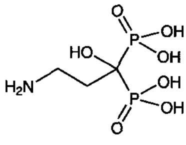
7002. Pamicogrel. [101001-34-7] 2-[4,5-Bis(4-methoxyphenyl)-2-thiazolyl]-1*H*-pyrrole-1-acetic acid ethyl ester; ethyl 2-[4,5-bis(*p*-methoxyphenyl)-2-thiazolyl]pyrrole-1-acetate; KB-3022; KBT-3022. $C_{25}H_{24}N_2O_4S$; mol wt 448.53. C 66.94%, H 5.39%, N 6.25%, O 14.27%, S 7.15%. Cyclooxygenase inhibitor. Prepn: K. Yoshino *et al.,* **EP 159677**; *eidem,* **US 4659726** (1985, 1987 both to Kanebo). HPLC determn in plasma and urine: Y. Nakada *et al., Chem. Pharm. Bull.* **38,** 1093 (1990). Pharmacokinetics: Y. Nakada *et al., Yakuzaigaku* **53,** 210 (1993), *C.A.* **120,** 315100 (1993). Activity as antithrombotic: K. Yokoto *et al., Jpn. J. Pharmacol.* **68,** 201 (1995); as platelet aggregation inhibitor: K. Yokoto *et al., J. Pharm. Pharmacol.* **47,** 768 (1995). Evaluation of cerebral protective effects: N. Yamamoto *et al., Jpn. J. Pharmacol.* **69,** 421 (1995); *eidem, Eur. J. Pharmacol.* **297,** 225 (1996).



Crystals from ligroin, mp 132.5-135.5°. LD_{50} orally in male mice: >3000 mg/kg (Yoshino).

THERAP CAT: Antithrombotic.

7003. Pamidronic Acid. [40391-99-9] (3-Amino-1-hydroxypropylidene)bisphosphonic acid; 3-amino-1-hydroxypropane-1,1-diphosphonic acid; ADP; AHPrBP. $C_3H_{11}NO_7P_2$; mol wt 235.07. C 15.33%, H 4.72%, N 5.96%, O 47.64%, P 26.35%. Bisphosphonate antiresorptive agent. Prepn: F. Krueger *et al.*, **DE 2130794** (1973 to Benckiser), *C.A.* **78,** 84528z (1973); K.-H. Worms *et al., Z. Anorg. Allg. Chem.* **457,** 214 (1979). Improved process: H. Blum, K.-H. Worms, **US 4327039** (1982 to Henkel). Mechanism of action study: P. M. Boonekamp *et al., Bone Miner.* **1,** 27 (1986). HPLC determn in serum and plasma: R. W. Sparidans *et al., J. Chromatogr. B* **705,** 331 (1998). Clinical trial to prevent postmenopausal bone loss: B. Lees *et al., Osteoporos. Int.* **6,** 480 (1996). Review of pharmacology and therapeutic use in resorptive bone disease: A. Fitton, D. McTavish, *Drugs* **41,** 289-318 (1991); A. J. Coukell, A. Markham, *Drugs Aging* **12,** 149-168 (1998).



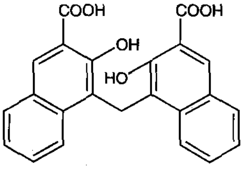
Disodium salt. [57248-88-1] Pamidronate disodium; GCP-23339A; Aminomux; Aredia. $C_3H_9NNa_2O_7P_2$; mol wt 279.03.

THERAP CAT: Bone resorption inhibitor.

7004. Pamiteplase. 275-L-Glutamic acid (1-91)-(174-527)-plasminogen activator (human tissue-type protein moiety); YM-866; Solinase. Genetically engineered variant of human tissue plasminogen activator (t-PA), *q.v.* Derived by deletion of the first kringle domain and the substitution of glutamic acid for arginine at position 275. Prepn: Y. Kawauchi *et al.*, **WO 8903874**; *eidem*, **US 5556621** (1989, 1996 both to Yamanouchi). Thrombolytic activity: T. Kawasaki *et al., Jpn. J. Pharmacol.* **63,** 9 (1993); M. Suzuki *et al., Curr. Ther. Res.* **61,** 7 (2000). Toxicology: A. Ishikawa *et al., J. Toxicol. Sci.* **22,** 117 (1997). Review of thrombolytic agents: M. Verstraete, *Am. J. Med.* **109,** 52-58 (2000).

THERAP CAT: Thrombolytic.

7005. Pamoic Acid. [130-85-8] 4,4′-Methylenebis[3-hydroxy-2-naphthalenecarboxylic acid]; 4,4′-methylenebis(3-hydroxy-2-naphthoic acid); 4,4′-methylenedi(3-hydroxy-2-naphthoic acid); 2,2′-dihydroxy-1,1′-dinaphthylmethane-3,3′-dicarboxylic acid; embonic acid. $C_{23}H_{16}O_6$; mol wt 388.37. C 71.13%, H 4.15%, O 24.72%. Prepn from 2-hydroxy-3-naphthoic acid + formaldehyde: Strohback, *Ber.* **34,** 4162 (1901); Brass, Sommer, *ibid.* **61,** 993 (1928); Barber, Gaimster, *J. Appl. Chem.* **2,** 565 (1952). Prepn of salts: Puetzer, **US 2397903** (1946 to Vick Chem.); Barber, **US 2641610** (1953 to May & Baker).



Crystals from dil pyridine, dec above 280° without melting. Practically insoluble in water, alcohol, ether, benzene, acetic acid. Sparingly sol in chloroform; sol in nitrobenzene, pyridine.

Methyl ether. $C_{24}H_{18}O_6$. Yellow crystals from dil methanol, dec 277-282°.

7006. Pancreatic Extract. Pancreas powder; Creon; Ku-Zyme; Pancrease; Pancrex-Vet; Panzytrat; Ultrase; Viokase. Substance prepd from fresh or frozen mammalian pancreas, usually from swine, that contains various enzymes having proteolytic, lipolytic and amylolytic activities. Pharmacopeial specifications differ on the quantity of amylase, lipase and protease required; most commercial formulations are of higher digestive power. Method of production from cow or pig pancreas: S. Hoek, **US 3223594** (1965 to N. American Philips). Clinical pharmacology and comparison of formulations: Y. W. Cho, D. M. Aviado, *J. Clin. Pharmacol.* **21,** 224 (1981). Analysis of pharmaceutical preparations: C. L. Case *et al., Pancreas* **30,** 180 (2005). Clinical trial in weight loss prevention in pancreatic cancer: M. J. Bruno *et al., Gut* **42,** 92 (1998); in cystic fibrosis: R. C. Stern *et al., Am. J. Gastroenterol.* **95,** 1932 (2000); C. J. Patchell *et al., J. Cyst. Fibr.* **1,** 287 (2002).

Slightly brown, amorphous powder. Partly sol in water. Practically insol in alcohol, ether.

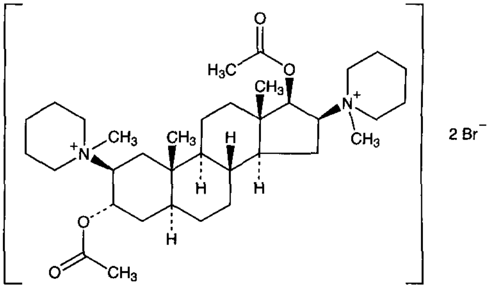
Pancreatin. [8049-47-6] Pancreatic enzyme concentrate containing not less than 2 USP units of lipase, 25 of amylase and 25 of protease activities per mg. British Pharmacopeia specifies not less than 20 FIP units of lipase, 24 of amylase and 1.4 of protease activities per mg.

Pancrelipase. [53608-75-6] Porcine pancreatic enzyme concentrate containing not less than 24 USP units of lipase, 100 of amylase and 100 of protease activities per mg.

THERAP CAT: Enzyme replacement therapy (pancreatic exocrine insufficiency).

THERAP CAT (VET): Enzyme replacement therapy in pancreatic enzyme deficiency.

7007. Pancuronium Bromide. [15500-66-0] 1,1′-[(2β,3α,5α,16β,17β)-3,17-Bis(acetyloxy)androstane-2,16-diyl]bis[1-methylpiperidinium] dibromide; 1,1′-(3α,17β-dihydroxy-5α-androstan-2β,16β-ylene)bis[1-methylpiperidinium] dibromide diacetate; 3α,17β-diacetoxy-2β,16β-dipiperidino-5α-androstane dimethobromide; 2β,16β-dipiperidino-5α-androstane-3α,17β-diol diacetate dimethobromide; poncuronium bromide (rescinded USAN); NA-97; Org-NA-97; Mioblock; Pavulon. $C_{35}H_{60}Br_2N_2O_4$; mol wt 732.67. C 57.38%, H 8.25%, Br 21.81%, N 3.82%, O 8.73%. Aminosteroid, competitive neuromuscular blocker. Prepn: W. R. Buckett *et al., Chim. Ther.* **2,** 186 (1967); *eidem, J. Med. Chem.* **16,** 1116 (1973). Structural studies: Savage *et al., J. Chem. Soc. B* **1971,** 410. Structure-activity correlation: Waser, *Anaesthesist* **20,** 23 (1971). Pharmacology: W. R. Buckett, I. L. Bonta, *Fed. Proc.* **25,** 718 (1966); W. R. Buckett *et al., Br. J. Pharmacol. Chemother.* **32,** 671 (1968); I. L. Bonta *et al., Eur. J. Pharmacol.* **4,** 83, 303 (1968). Comparative study of neuromuscular blocking and vagolytic effect: S. L. Son *et al., Anesthesiology* **55,** 12 (1981). *Review:* Speight, Avery, *Drugs* **4,** 163-226 (1972).



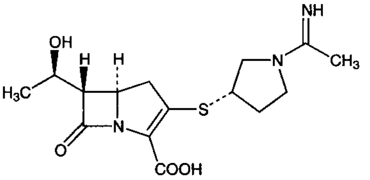
Odorless crystals with bitter taste, mp 215°. One gram dissolves in 30 parts chloroform, one part water (20°). LD_{50} in mice (mg/kg): 0.047 i.v.; 0.152 i.p.; 0.167 s.c.; 21.9 orally; in rats, rabbits: 0.153, 0.016 i.v. (Buckett, 1968).

THERAP CAT: Neuromuscular blocking agent.

THERAP CAT (VET): Neuromuscular blocking agent.

7008. Pangamic Acid. Controversial mixture of compounds erroneously labeled as ***vitamin B_{15}***. Allegedly isolated from apricot kernel: E. T. Krebs, Sr. *et al., Int. Rec. Med.* **164,** 18 (1951). Originally named pangamic acid because of its supposed ubiquity in seeds. There is no clear chemical identity for pangamic acid. An historical review by J. C. Micheau *et al.*, in *Chim. Ther.* **7,** 103 (1972) contains structural studies, analyses, syntheses and discussion of various components of pangamic acid. Products sold as pangamic acid in the U.S. vary considerably in their composition. Some are mixtures of calcium gluconate and *N,N*-dimethylglycine, *q.q.v.*; others contain diisopropylamine dichloroacetate, *q.v.*: *FDA Drug Bulletin* **vol. 8**(6), Dec. 1978-Jan. 1979. *Ref.:* V. Herbert, *Am. J. Clin. Nutr.* **32,** 1534 (1979); V. Herbert, R. Herbert, in *Controversies in Nutrition,* L. Ellenbogen, Ed. (Churchill-Livingstone, New York, 1981) pp 159-170.

7009. Panipenem. [87726-17-8] (5*R*,6*S*)-6-[(1*R*)-1-Hydroxyethyl]-3-[[(3*S*)-1-(1-iminoethyl)-3-pyrrolidinyl]thio]-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid; (5*R*,6*S*)-6-[(*R*)-1-hydroxyethyl]-2-[(*S*)-1-acetimidoylpyrrolidin-3-ylthio]-1-carbapen-2-em-3-carboxylic acid; (+)-(5*R*,6*S*)-3-[[(*S*)-1-acetimidoyl-3-pyrrolidinyl]thio]-6-[(*R*)-1-hydroxyethyl]-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid; CS-533; RS-533. $C_{15}H_{21}N_3O_4S$; mol wt 339.41. C 53.08%, H 6.24%, N 12.38%, O 18.86%, S 9.45%. Carbapenem antibiotic. Prepn: T. Miyadera *et al., J. Antibiot.* **36,** 1034 (1983). Manufacturing process: A. Yoshida, K. Oda, **EP 587436** (1994 to Sankyo). Antibacterial spectrum *in vitro:* H. C. Neu *et al., Antimicrob. Agents Chemother.* **30,** 828 (1986). Series of articles on pharmacology and clinical efficacy in combination with betamipron, *q.v.: Chemotherapy (Tokyo)* **39** Suppl 3, 1-813 (1991). Toxicology: K. Kimura *et al., ibid.* 140.



Prepd as the hemihydrate; colorless fine prisms, mp 198-200° (dec). uv max (water): 298 nm (ε 10400). Approx LD_{50} in male, female mice (mg/kg): 1700-2200, 1300-1700 i.v. (Kimura).

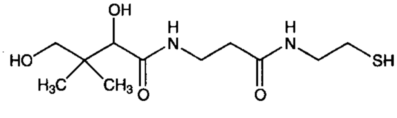
Mixture with betamipron. [138240-65-0] CS-976; Carbenin.

THERAP CAT: Antibacterial.

7010. Panitumumab. [339177-26-3] Anti-(human epidermal growth factor receptor) immunoglobulin (human monoclonal ABX-EGF heavy chain) disulfide with human monoclonal ABX-EGF light chain, dimer; ABX-EGF. Fully human monoclonal antibody secreted by the E7.6.3 hybridoma; directed against human epidermal growth factor receptor (EGFr), a transmembrane cell-surface glycoprotein overexpressed in a variety of cancers. Prepn: A. Jakobovits *et al.,* **WO 9850433;** *eidem,* **US 6235883** (1998, 2001 both to Abgenix); and *in vivo* antitumor activity: X.-D. Yang *et al., Cancer Res.* **59,** 1236 (1999). Clinical pharmacokinetics: E. K. Rowinsky *et al., J. Clin. Oncol.* **22,** 3003 (2004). Review of preclinical and clinical evaluations: K. A. Foon *et al., Int. J. Radiat. Oncol. Biol. Phys.* **58,** 984-990 (2004).

THERAP CAT: Antineoplastic.

7011. Pantetheine. [496-65-1] 2,4-Dihydroxy-*N*-[3-[(2-mercaptoethyl)amino]-3-oxopropyl]-3,3-dimethylbutanamide; 2,4-dihydroxy-*N*-[2-[(2-mercaptoethyl)carbamoyl]ethyl]-3,3-dimethylbutyramide; *N*-(pantothenyl)-β-aminoethanethiol; α,γ-dihydroxy-β,β-dimethylbutyryl-β-alanyl-β-aminoethanethiol. $C_{11}H_{22}N_2O_4S$; mol wt 278.37. C 47.46%, H 7.97%, N 10.06%, O 22.99%, S 11.52%. Growth factor for *Lactobacillus bulgaricus:* Williams *et al., J. Biol. Chem.* **177,** 933 (1949). Intermediate in the pathway of coenzyme A, *q.v.,* formation in mammalian liver and in some microorganisms. Synthesis: Schwyzer, *Helv. Chim. Acta* **35,** 1903 (1952); Baddiley, Thain, *J. Chem. Soc.* **1952,** 800; King *et al., J. Am. Chem. Soc.* **75,** 1290 (1953); Walton *et al., ibid.* **76,** 1146 (1954); Walton, **US 2744119** and **US 2835704** (1956, 1958, both to Merck & Co.). *Reviews:* Snell, Brown, *Adv. Enzymol.* **14,** 49 (1953); Snell, Wittle, *Methods Enzymol.* **3,** 918 (1957).



Syrup or glass. $[\alpha]_D^{20}$ +12.9° (c = 4.5 in water). Microbiological activity: 20,000 LBF units/mg. An LBF unit is that amount of the growth factor contained in one mg of Basamine-Busch, a standard yeast extract manuf by Anheuser-Busch, Inc.

Silver mercaptide. $C_{11}H_{21}AgN_2O_4S$. Yellow noncryst solid. $[\alpha]_D^{25}$ +8° (c = 4.27 in 0.9*N* NaCl). Very sol in water. 11,000 LBF units/mg.

Mercuric mercaptide. $C_{22}H_{42}HgN_4O_8S_2.C_3H_6O$. Crystals from acetone, mp 96-98°. $[\alpha]_D^{27}$ +9.6° (c = 4 in water). 15,500 LBF units/mg. uv max: 260-265 nm (ε 1000). Sol in water, methanol.

***S*-Benzoylpantetheine.** $C_{18}H_{26}N_2O_5S$. Crystals from ethyl acetate, mp 116°. $[\alpha]_D^{27}$ +31° (ethanol). Sol in water, ethyl acetate, chloroform.

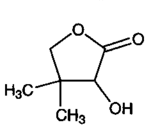
***S*-Acetylpantetheine.** $C_{13}H_{24}N_2O_5S$. Thick syrup. $[\alpha]_D^{27}$ +39° (c = 0.8 in ethanol).

7012. Pantethine. [16816-67-4] *N,N′*-[Dithiobis[2,1-ethanediylimino(3-oxo-3,1-propanediyl)]]bis[2,4-dihydroxy-3,3-dimethylbutanamide]; *N,N′*-[dithiobis(ethyleneiminocarbonylethylene)]bis(2,4-dihydroxy-3,3-dimethylbutyramide); D-bis(*N*-pantothenyl-β-aminoethyl) disulfide; Lipodel; Pantetina; Panthecin; Pantomin; Pantosin. $C_{22}H_{42}N_4O_8S_2$; mol wt 554.72. C 47.63%, H 7.63%, N 10.10%, O 23.07%, S 11.56%. $[HOCH_2C(CH_3)_2CHOHCONHCH_2CH_2CONHCH_2CH_2S]_2$. Disulfide dimer of pantetheine, *q.v.* Growth factor for *Lactobacillus bulgaricus:* Williams *et al., J. Biol. Chem.* **177,** 933 (1949). Formed by oxidation of pantetheine: Brown, Snell, *J. Biol. Chem.* **198,** 375 (1952). Structure: Snell *et al., J. Am. Chem. Soc.* **72,** 5349 (1950). Synthesis: Wieland, Bokelmann, *Naturwissenschaften* **38,** 384 (1951); Wittle *et al., J. Am. Chem. Soc.* **75,** 1694 (1953); Viscontini *et al., Helv. Chim. Acta* **37,** 375 (1954); Bowman, Cavalla, *J. Chem. Soc.* **1954,** 1171; Shimizu *et al., Chem. Pharm. Bull.* **13,** 180 (1965). Clinical trial in hyperlipoproteinemia: A. Gaddi *et al., Atherosclerosis* **50,** 73 (1984).

Glassy, colorless to light yellow substance. $[\alpha]_D^{27}$ +13.5° (c = 3.75 in water). Freely sol in water; less sol in ethanol. Practically insol in ether, acetone, ethyl acetate, benzene, chloroform.

THERAP CAT: Antilipemic.

7013. Pantolactone. [599-04-2] Dihydro-3-hydroxy-4*H*-dimethyl-2(3*H*)-furanone; pantoic acid γ-lactone; pantoyl lactone; pantoic lactone; 2,4-dihydroxy-3,3-dimethylbutyric acid γ-lactone; α-hydroxy-β,β-dimethyl-γ-butyrolactone. $C_6H_{10}O_3$; mol wt 130.14. C 55.37%, H 7.75%, O 36.88%. A degradation product of pantothenic acid from liver: Williams, Major, *Science* **91,** 246 (1940). Important intermediate in the synthesis of pantothenic acid. May be prepd by condensing isobutyraldehyde with formaldehyde yielding α,α-dimethyl-β-hydroxypropionaldehyde which is condensed with hydrocyanic acid in the presence of calcium chloride to form racemic pantolactone. Various modifications of this procedure exist: Glaser, *Monatsh. Chem.* **25,** 46 (1904); Stiller *et al., J. Am. Chem. Soc.* **62,** 1785 (1940); Reichstein, Grüssner, *Helv. Chim. Acta* **23,** 650 (1940); Carter, Ney, *J. Am. Chem. Soc.* **63,** 312 (1941). Vast patent literature, *e.g.,* Beckmann *et al.;* Klein, **US 2967869** and **US 3024250** (1961, 1962, both to Nopco).



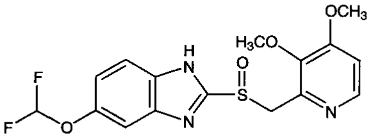
D(−)-Form. Hygroscopic crystals from benzene + petr ether, mp 92°. $[\alpha]_D^{25}$ −50.7° (c = 2.05 in H_2O). Can be purified by microsublimation.

L(+)-Form. Hygroscopic crystals from benzene, mp 91°. $[\alpha]_D^{25}$ +50.1° (c = 2 in H_2O).

DL-Form. Hygroscopic rosettes or prisms, mp 80°, bp_{18} 130°. Freely sol in water. Sol in ether, benzene, chloroform, alcohol, carbon disulfide.

7014. Pantoprazole. [102625-70-7] 5-(Difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridinyl)methyl]sulfinyl]-1*H*-benzimidazole; SKF-96022; BY-1023. $C_{16}H_{15}F_2N_3O_4S$; mol wt 383.37. C 50.13%, H 3.94%, F 9.91%, N 10.96%, O 16.69%, S 8.36%. Gastric proton pump inhibitor. Prepn: B. Kohl *et al.,* **EP 166287;** *eidem,* **US 4758579** (1986, 1988 both to Byk Gulden); *eidem, J. Med. Chem.* **35,** 1049 (1992). Mechanism of action: W. A. Simon *et al., Biochem. Pharmacol.* **39,** 1799 (1990).

HPLC determn in plasma and serum: R. Huber *et al., J. Chromatogr.* **529,** 389 (1990). Clinical pharmacokinetics: B. Simon *et al., Z. Gastroenterol.* **28,** 443 (1990). Clinical trial in duodenal ulcer: P. Müller *et al., ibid.* **30,** 771 (1992); in Zollinger-Ellison syndrome: E. A. Lew *et al., Gastroenterology* **118,** 696 (2000). Review of pharmacology and clinical experience: P. Poole, *Am. J. Health-Syst. Pharm.* **58,** 999-1008 (2001).

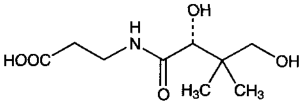


Off-white solid, mp 139-140° (dec). pKa$_1$ 3.92; pKa$_2$ 8.19.

Sodium salt. [138786-67-1] Eupantol; Pantecta; Pantozol; Pantopan; Pantorc; Peptazol; Protium; Protonix; Somac. $C_{16}H_{14}F_2N_3NaO_4S$; mol wt 405.35. Prepd as the sesquihydrate. White to off-white crystalline powder, dec >130°. uv max (methanol): 289 (ε 1.64×10^4). Freely sol in water; very slightly sol in phosphate buffer (pH 7.4). Practically insol in *n*-hexane.

THERAP CAT: Antiulcerative; in treatment of Zollinger-Ellison syndrome.

7015. Pantothenic Acid. [79-83-4] *N*-[(2*R*)-2,4-Dihydroxy-3,3-dimethyl-1-oxobutyl]-β-alanine; D(+)-*N*-(2,4-dihydroxy-3,3-dimethylbutyryl)-β-alanine; chick antidermatitis factor; vitamin B$_5$. $C_9H_{17}NO_5$; mol wt 219.23. C 49.31%, H 7.82%, N 6.39%, O 36.49%. A member of the B complex vitamins; essential vitamin for the biosynthesis of coenzyme A in mammalian cells. Occurs ubiquitously in all animal and plant tissue. The richest common source is liver, but jelly of the queen bee contains 6 times as much as liver. Rice bran and molasses are other good sources. Isoln from liver: R. J. Williams *et al., J. Am. Chem. Soc.* **60,** 2719 (1938). Synthesis: E. T. Stiller *et al., ibid.* **62,** 1785 (1940); Reichstein, Grüssner, *Helv. Chim. Acta* **23,** 650 (1940); Grüssner *et al., ibid.* 1276. Absolute configuration: Hill, Chan, *Biochem. Biophys. Res. Commun.* **38,** 181 (1970). Only the natural, dextrorotatory form has vitamin activity. Review of chemistry, biochemistry and pharmacology: W. Friedrich, *Vitamins* (de Gruyter, Berlin, 1988) pp 809-835; of metabolism: A. G. Tahiliani, C. J. Beinlich, *Vitam. Horm.* **46,** 165-228 (1991).



Unstable, viscous oil. Extremely hygroscopic. Easily destroyed by acids, bases, heat. $[\alpha]_D^{25}$ +37.5°. Freely sol in water, ethyl acetate, dioxane, glacial acetic acid; moderately sol in ether, amyl alcohol. Practically insol in benzene, chloroform.

Sodium salt. [867-81-2] $C_9H_{16}NNaO_5$. Very hygroscopic crystals. $[\alpha]_D^{25}$ +27.1° (c = 2). Can be stored in sealed ampuls only.

Calcium salt. [137-08-6] Calpanate; Pantholin. $C_{18}H_{32}CaN_2O_{10}$; mol wt 476.53. Prepn: Wehrmeister, **US 2780645** (1957 to Commercial Solvents); Kagan, **US 2845456** (1958 to Upjohn). Minute needles from CH_3OH. Sweetish taste with slightly bitter aftertaste. Dec 195-196°. Moderately hygroscopic. $[\alpha]_D^{20}$ +28.2° (c = 5). One gram dissolves in 2.8 ml H_2O. Sol in glycerol; slightly sol in alcohol, acetone. pH of 5% aq soln: 7.2-8.0; pH in CO_2-free water: 8.7.

THERAP CAT: Vitamin.

THERAP CAT (VET): Nutritional factor: dietary essential except in horses, ruminants.

7016. Papain. [9001-73-4] Papayotin; vegetable pepsin; Arbuz; Nematolyt; Summetrin; Tromasin; Velardon; Vermizym. First recognized member of the class of proteolytic enzymes that needs a free sulfhydryl group for activity. Isolated from the latex of the green fruit and leaves of *Carica papaya* L., *Caricaceae.* Initial isolation and crystallization: Balls *et al., Science* **86,** 379 (1937); Balls, Lineweaver, *J. Biol. Chem.* **130,** 669 (1939). Prepn from commercial dried papaya latex and physical properties: Kimmel, Smith, *ibid.* **207,** 515 (1954); *see also ibid.* 533-573; Becker, *Econ. Bot.* **12,** 62 (1958). Purification: Gibian, Bratfisch, **US 2950227** (1960 to Schering AG); Lesuk, **US 3011952** (1961 to Sterling Drug); Blumberg *et al., Eur. J. Biochem.* **15,** 97 (1970). The papain molecule consists of one folded polypeptide chain of 212 residues, mol wt ~23,400. Complete amino acid sequence: Drenth *et al., Nature* **218,** 929 (1968); Mitchel *et al., J. Biol. Chem.* **245,** 3485 (1970). Mechanism of action studies: Morihara, *J. Biochem.* **62,** 250 (1967). Use in treatment of contact lenses to prolong wearing time in keratoconic patients with papillary conjunctivitis: D. R. Korb *et al., Arch. Ophthalmol.* **101,** 48 (1983). *Reviews:* Kimmel, Smith in *Adv. Enzymol. Relat. Subj. Biochem.* **19,** 267-334 (1957); Glazer, Smith in *The Enzymes* **vol. III,** P. D. Boyer, Ed. (Academic Press, New York, 3rd ed., 1971) pp 501-537; *see also* Drenth *et al., ibid.* 485-498 and *eidem, Adv. Protein Chem.* **25,** 79-115 (1971) for a comprehensive review of the structural elucidation.

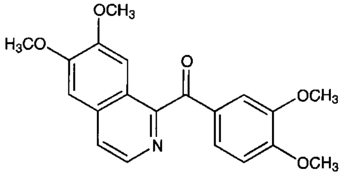
White or grayish-white, slightly hygroscopic powder. uv max: 278 nm ($A_{1cm}^{1\%}$ 25.0). Incompletely sol in water, glycerol. Practically insol in most organic solvents. *Keep well closed.* Potency varies according to process of prepn, etc. with the usual grade digesting ~35 times its wt of lean meat. Best grades render sol 200-300 times their wt of coagulated egg albumin in alkaline media. A temp. range of 60-90° is favorable for the digestive process with 65° the optimum point. Best pH is 5.0, but it functions also in neutral or alkaline media. Activated by reduction (HCN, H_2S etc.) and inactivated by oxidation (H_2O_2, iodoacetate).

Note: The term papain is currently applied to both the crude dried latex and the crystalline proteolytic enzyme.

USE: For tenderizing meats; for clearing beverages; for bating skins.

THERAP CAT: Enzyme (proteolytic). Debriding agent; digestive aid. Has been used to prevent adhesions; as anthelmintic (Nematodes).

7017. Papaveraldine. [522-57-6] (6,7-Dimethoxy-1-isoquinolinyl)(3,4-dimethoxyphenyl)methanone; 6,7-dimethoxy-1-isoquinolyl 3,4-dimethoxyphenyl ketone; 6,7-dimethoxy-1-veratroylisoquinoline; xanthaline. $C_{20}H_{19}NO_5$; mol wt 353.37. C 67.98%, H 5.42%, N 3.96%, O 22.64%. The old name papaveraldine is retained to avoid confusion. From opium; whether papaveraldine occurs as such in the poppy plant, or is formed during the process of extraction, has not been investigated. Oxidation of papaverine to papaveraldine by SeO_2: Menon, *Proc. Indian Acad. Sci.* **19A,** 21 (1944). For older references *see:* Small, Lutz, "Chemistry of the Opium Alkaloids," in *U.S. Public Health Reports* **Suppl. No. 103** (Washington, 1932). Synthesis from Reissert compds: Popp, McEwen, *J. Am. Chem. Soc.* **79,** 3773 (1957).



Crystals from abs ethanol, mp 208-209°. Sol in benzene, chloroform; slightly sol in alcohol, ether, petr ether; nearly insol in water, alkalies or carbonates.

Hydrochloride. $C_{20}H_{19}NO_5.HCl$. Yellow crystals from abs alcohol, mp 200°.

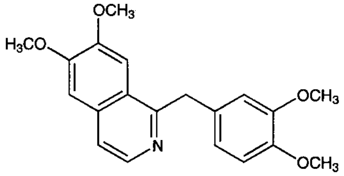
7018. Papaveretum. [8002-76-4] "Concentrated opium"; Omnopon; Pantopon. A mixture of the hydrochlorides of the opium alkaloids in their approximate natural proportions. Contains approx 50% morphine, 3% codeine, 20% noscapine, and 5% papaverine. Exhibits biological action of morphine and other alkaloids present in opium. Clinical evaluation in intravenous analgesia: J. A. Catling *et al., Br. Med. J.* **281,** 478 (1980).

Yellowish-gray, cryst powder. Freely sol in water.

Note: This is a controlled substance (opium derivative): **21 CFR,** 1308.12.

THERAP CAT: Analgesic (narcotic).

7019. Papaverine. [58-74-2] 1-[(3,4-Dimethoxyphenyl)-methyl]-6,7-dimethoxyisoquinoline; 6,7-dimethoxy-1-veratrylisoquinoline. $C_{20}H_{21}NO_4$; mol wt 339.39. C 70.78%, H 6.24%, N 4.13%, O 18.86%. Smooth muscle relaxant found in opium (0.8-1.0%). Synthesis: Pictet, Gams, *Compt. Rend.* **149,** 210 (1909); *Ber.* **42,** 2943 (1909). Review of commercial syntheses: Goldberg, *Chem. Prod. Chem. News* **17,** 371 (1954). Improved synthetic procedures: Braz, Chizhov, *Soviet Pharmaceutical Research* **3,** 90-93 (New York, 1958). Biosynthetic studies: Battersby, Harper, *J. Chem. Soc.* **1962,** 3526; Brochmann-Hanssen *et al., J. Pharm. Sci.* **60,** 1672 (1971). Pharmacology and toxicology: Preininger in *The Alkaloids* **vol. 15,** R. H. F. Manske, Ed. (Academic Press, New York, 1975) pp 209-223. Toxicity: S. Levis *et al., Arch. Int. Pharmacodyn.* **123,** 264 (1960). Clinical effect on cerebral blood flow: H. L. Karpman, J. J. Sheppard, *Angiology* **26,** 592 (1975). Clinical evaluation in intermittent claudication: Y. Sheino *et al., ibid.* **34,** 257 (1983). Comprehensive description: M. S. Hifnawy, F. J. Muhtadi, *Anal. Profiles Drug Subs.* **17,** 367-447 (1988).



Triboluminescent, orthorhombic prisms from alcohol + ether, mp 147°. Sublimes at 135-140° at 11 mm pressure and 2 mm distance. d_4^{20} 1.337. pK (25°) 8.07. uv max (ethanol): 239, 278-280, 314, 327 nm (log ε 4.83, 3.86, 3.60, 3.67). Almost insol in water. Sol in hot benzene, glacial acetic acid, acetone; slightly sol in chloroform, carbon tetrachloride, petr ether. Optimal pH for storage of papaverine solns: 2.0-2.8.

Hydrochloride. [61-25-6] Artegodan; Cepaverin; Cerebid; Cerespan; Dynovas; Optenyl; Pameion; Panergon; Papital T.R.; Pavabid; Pavacen; Pavadel; Pavagen; Pavakey; Pavased; Spasmo-Nit; Therapav; Vasal; Vasospan. $C_{20}H_{21}NO_4.HCl$; mol wt 375.85. Monoclinic rods from water, mp 220-225°. uv max (ethanol): 249-250, 280-282, 311 nm (log ε 4.69, 3.80, 3.82). One gram dissolves in about 40 ml water. Sol in alcohol and chloroform. Practically insol in ether. pH of 0.05 molar soln 3.9; pH of 2% aq soln 3.3. LD_{50} in mice, rats (mg/kg): 27.5, 20 i.v.; 150, 370 s.c. (Levis).

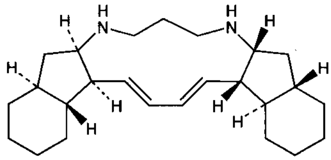
Nitrite. [132-40-1] $C_{20}H_{21}NO_4.HNO_2$. Light yellow, crystalline powder. Slightly soluble in water or alcohol; freely sol in chloroform, acetone.

THERAP CAT: Vasodilator (cerebral).

7020. Papaya. Papaw; Carica; melon tree. Fruit of *Carica papaya* L., *Caricaceae. Habit.* Tropical America and Asia, Florida. *Constit.* Papain, the dried and purified latex of the fruit; carpaine; carposide (a glucoside).

USE: Manufacture of papain.

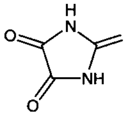
7021. Papuamine. [112455-84-2] (4a*S*,5a*R*,10a*R*,11a*S*,15a*R*,15b*S*,16*E*,18*E*,19a*S*,19b*R*)-2,3,4,4a,5,5a,6,7,8,9,10,10a,11,11a,12,13,14,15,15a,15b,19a,19b-Docosahydro-1*H*-diindeno[2,1-*f*:1′,2′-1][1,5]diazacyclotridecine. $C_{25}H_{40}N_2$; mol wt 368.60. C 81.46%, H 10.94%, N 7.60%. Alkaloid originally isolated from *Haliclona sp.*, a marine sponge found in Papua, New Guinea. Exhibits antifungal and antimicrobial activity. Isoln and characterization: B. J. Baker *et al., J. Am. Chem. Soc.* **110,** 965 (1988). Total synthesis: R. M. Borzilleri *et al., ibid.* **116,** 9789 (1994).



White solid, mp 167.5-169°. $[\alpha]_D$ −150° (c = 1.5 in methanol).

Dihydrochloride. [112347-74-7] White solid, mp 230° (dec). $[\alpha]_D$ −140° (c = 1.3 in CH_3OH). uv max (methanol): 241 nm (ε 3000).

7022. Parabanic Acid. [120-89-8] Imidazolidinetrione; imidazoletrione; oxalylurea. $C_3H_2N_2O_3$; mol wt 114.06. C 31.59%, H 1.77%, N 24.56%, O 42.08%. Prepd by the condensation of urea with diethyl oxalate in a methanol soln of sodium methoxide: Murray, *Org. Synth.* **37,** 71 (1957).



Crystals, mp about 230°; also stated as 243° with decomposition. Sublimes at 100°. Soluble in about 20 parts water, in alcohol. Its salts are unstable.

7023. Paraffin. Paraffin wax; hard paraffin. A mixture of solid hydrocarbons having the general formula C_nH_{2n+2}, obtained from petroleum.

Colorless or white, somewhat translucent, odorless mass; greasy feel; burns with a luminous flame. d about 0.90. mp 50-57°; also available with higher and lower melting ranges. Insol in water or alcohol. Sol in benzene, chloroform, ether, carbon disulfide, oils; miscible when melted with wax, spermaceti, fats.

Caution: Potential symptoms of overexposure to fumes are irritation of eyes, skin, respiratory system; discomfort and nausea. *See NIOSH Pocket Guide to Chemical Hazards* (DHHS/NIOSH 97-140, 1997) p 240.

USE: For raising mp of ointments. Manuf paraffin paper and candles (so-called wax paper or candles); for fixing drawings, etc., on muslin; water-proofing wood, cork, paper, leather; manuf varnishes; to render wooden vessels impermeable to water or alcohol; in lubricants; to cover food products; in floor polishes, cosmetics, electrical insulators; for extracting perfumes from flowers. Pharmaceutic aid (stiffening agent).

7024. Paraffin Chlorinated. Chlorcosane; Cereclor. Prepared by chlorinating a liquid paraffin. Contains about 50% Cl.

Light yellow to amber, thick, oily liq; odorless and stable in air. d 1.00-1.07. Insol in water. Slightly sol in alc; miscible with benzene, chloroform, ether, carbon tetrachloride.

Caution: Chlorinated paraffins (C_{12}, 60% Cl) are reasonably anticipated to be human carcinogens: *Report on Carcinogens, Eleventh Edition* (PB2005-104914, 2004) p III-51.

USE: As solvent for dichloramine-T, dissolving about 8%.

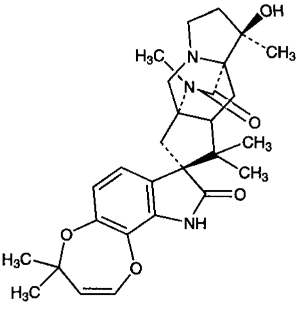
7025. Paraformaldehyde. [30525-89-4] Polyoxymethylene; Paraform; Formagene. Also erroneously referred to as ***Triformol*** or as ***"trioxymethylene"***. Polymerized formaldehyde, $(CH_2O)_n$. Obtained by concentrating formaldehyde soln. Use in mummifying dental pulp: I. Curson, *Br. Dent. J.* **121,** 519 (1966); P. Hobson, *ibid.* **128,** 275 (1970).

White, cryst powder, having an odor of formaldehyde. Slowly sol in cold, more readily in hot water, with evolution of formaldehyde; insol in alcohol, ether; sol in fixed alkali hydroxide solns. *Keep tightly closed.*

USE: For disinfecting sickrooms, clothing, linen, and sickroom utensils. Active ingredient of contraceptive creams. Also used as fumigant; in dentistry; in manuf synthetic resins and artificial horn or ivory.

7026. Paraherquamide. [77392-58-6] (−)-Paraherquamide; [1′*R*-(1′α,5′aβ,7′β,8′aβ,9′aβ)]-2′,3′,8′a,9′-tetrahydro-1′-hydroxy-1′,4,4,8′,8′,11′-hexamethylspiro[4*H*,8*H*-[1,4]dioxepino[2,3-*g*]indole-8,7′(8′*H*)-[5*H*,6*H*-5a,9a](iminomethano)[1*H*]cyclopent[*f*]indolizine]-9,10′(10*H*)-dione. $C_{28}H_{35}N_3O_5$; mol wt 493.59. C 68.13%, H 7.15%, N 8.51%, O 16.21%. Oxindole alkaloid fungal metabolite. Isolation from *Penicillium paraherquei* and structure: M. Yamazaki *et al., Maikotokishin* **10,** 27 (1980), *C.A.* **95,** 19321p (1981); M. Yamazaki *et al., Tetrahedron Lett.* **22,** 135 (1981); from *P. charlesii* and nematocidal activity: J. G. Ondeyka *et al., J. Antibiot.* **43,** 1375 (1990). Absolute stereochemistry: T. A. Blizzard *et al., J. Org. Chem.* **54,** 2657 (1989). Approach to synthesis: R. M. Williams, T. D. Cushing, *Tetrahedron Lett.* **31,** 6325 (1990). Anthelmintic activity in sheep: W. L. Shoop *et al., J. Parasitol.* **76,** 349 (1990); in dogs: W. L. Shoop *et al., Vet.*

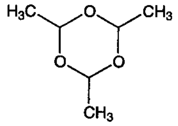
Parasitol. **40,** 339 (1991). Toxicity: *eidem, Am. J. Vet. Res.* **53,** 2032 (1992). Mode of action: J. M. Schaeffer *et al., Biochem. Pharmacol.* **43,** 679 (1992).



Colorless prisms, mp 244-247° (dec). $[\alpha]_D^{22}$ −28° (c = 0.43 in methanol). uv max (ethanol): 226, 260, 290nm (ε 32400, 6100, 1600). Sol in methanol, ethyl acetate, acetone, DMSO. Practically insol in water.

THERAP CAT (VET): Anthelmintic.

7027. Paraldehyde. [123-63-7] 2,4,6-Trimethyl-1,3,5-trioxane; paracetaldehyde; Paral. $C_6H_{12}O_3$; mol wt 132.16. C 54.53%, H 9.15%, O 36.32%. A polymer of acetaldehyde. Prepd by the polymerization of acetaldehyde catalyzed by HCl and H_2SO_4 at medium to high temp: Kekulé, Zincke, *Ann.* **162,** 125 (1872); Baer, Mahan, **US 2864827** (1958 to Phillips). Toxicity data: Figot *et al., Acta Pharmacol. Toxicol.* **8,** 290 (1952).



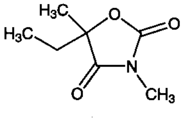
Liquid, characteristic aromatic odor and warm, but disagreeable taste. d_{25}^{25} ~0.994. bp ~124°. mp 12°. n_D^{20} 1.4049. Sol in 8 parts water at 25°, in 17 parts boiling water; miscible with alc, chloroform, ether, oils. Gives acetaldehyde on heating with dil HCl or on warming with several drops concd H_2SO_4. LD_{50} orally in rats: 1.65 g/kg (Figot).

Note: This is a controlled substance (depressant): **21 CFR,** 1308.14.

USE: Manuf organic compounds.

THERAP CAT: Sedative; hypnotic.

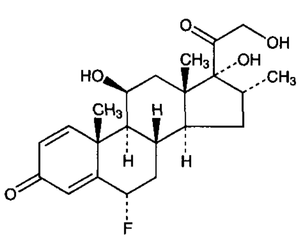
7028. Paramethadione. [115-67-3] 5-Ethyl-3,5-dimethyl-2,4-oxazolidinedione; 3,5-dimethyl-5-ethyloxazolidine-2,4-dione; Paradione. $C_7H_{11}NO_3$; mol wt 157.17. C 53.49%, H 7.05%, N 8.91%, O 30.54%. Prepn: Spielman, **US 2575693** (1951 to Abbott).



Liquid. Fruity, esterlike odor. d_4^{25} 1.1180-1.1240. n_D^{25} 1.449. Slightly sol in water. Freely sol in alcohol, benzene, chloroform, ether.

THERAP CAT: Anticonvulsant.

7029. Paramethasone. [53-33-8] (6α,11β,16α)-6-Fluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione; 6α-fluoro-16α-methylprednisolone; 16α-methyl-6α-fluoroprednisolone. $C_{22}H_{29}FO_5$; mol wt 392.46. C 67.33%, H 7.45%, F 4.84%, O 20.38%. Prepn: Edwards *et al., J. Am. Chem. Soc.* **82,** 2318 (1960). Toxicity study: E. I. Goldenthal, *Toxicol. Appl. Pharmacol.* **18,** 185 (1971).



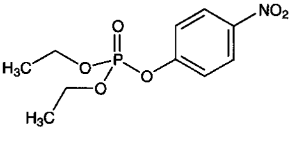
21-Acetate. [1597-82-6] Cortidene; Dilar; Dillar; Haldrate; Haldrone; Metilar; Monocortin; Paramezone; Syntecort; Stemex. $C_{24}H_{31}FO_6$; mol wt 434.50. mp 228-241° (dec). $[\alpha]_D$ +85°. uv max (ethanol): 243 nm (log ε 4.16). Sol in ethanol, acetone; slightly sol in water. LD_{50} i.p. in female rats: 392±23 mg/kg (Goldenthal).

Disodium phosphate. Soludillar.

Mixture of 21-acetate and disodium phosphate. Triniol.

THERAP CAT: Glucocorticoid.

7030. Paraoxon. [311-45-5] Phosphoric acid diethyl 4-nitrophenyl ester; diethyl *p*-nitrophenyl phosphate; phosphacol; E-600; Ester 25; Eticol; Fosfakol; Mintacol; Miotisal A; Soluglaucit. $C_{10}H_{14}NO_6P$; mol wt 275.20. C 43.64%, H 5.13%, N 5.09%, O 34.88%, P 11.26%. Prepd by the action of diethyl chlorophosphate on sodium *p*-nitrophenolate or by nitration of diethyl phenyl phosphate: Schrader, *BIOS Final Report* **No. 714,** 52 (1947); *Angew. Chem.* **62,** 471 (1950); **CH 257649** (1949); Fagerlind *et al., Sven. Farm. Tidskr.* **56,** 303, *C.A.* **46,** 9259. Physical properties: E. F. Williams, *Ind. Eng. Chem.* **43,** 950 (1951). Formation from parathion on citrus foliage and soil surface: R. C. Spear *et al., J. Agric. Food Chem.* **23,** 808 (1975); W. F. Spencer *et al., Bull. Environ. Contam. Toxicol.* **14,** 265 (1975). Toxicity study: W. R. Pickering, J. C. Malone, *Biochem. Pharmacol.* **16,** 1183 (1967). Brief review: G. Schrader, *Die Entwicklung neuer insektizider Phosphorsäure-Ester* (Verlag Chemie, Weinheim, 1963) pp 259-272.

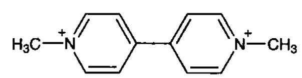


Oily liq. Slight odor. *Poisonous!* $bp_{1.0}$ 169-170°. d_4^{25} 1.2683. n_D^{20} 1.50959. uv max: 274 nm (ε 8.9×10³). Soly in water (25°): 2400 μg/mL. Freely sol in ether, other organic solvents. Aq solns are stable up to pH 7. Roughly 300 times more stable to hydrolysis than tetraethyl pyrophosphate. The uncatalyzed reaction with water is very small and the overall velocity constant is K = 0.52[OH] + 1×10^{-6} min^{-1}. *See:* Coates, *Ann. Appl. Biol.* **36,** 158 (1949). LD_{50} orally in rats: 1.8 mg/kg (Pickering, Malone).

Caution: Cholinesterase inhibitor. For symptoms *see* Parathion.

USE: Insecticide.

7031. Paraquat. [4685-14-7] 1,1′-Dimethyl-4,4′-bipyridinium; *N,N′*-dimethyl-γ,γ′-dipyridylium; methyl viologen (2+). $[C_{12}H_{14}N_2]^{2+}$. Non-selective contact herbicide. Prepn of dichloride and bismethyl sulfate derivs: L. Michaelis, E. S. Hill, *J. Am. Chem. Soc.* **55,** 1481 (1933); R. C. Brian *et al.,* **GB 813531** (1959 to ICI). Activity: R. F. Homer *et al., J. Sci. Food Agric.* **11,** 309 (1960); A. D. Dodge, *Endeavour* **30,** 130 (1971). Degradation: A. Calderbank, P. Slade, *Outlook Agric.* **5,** 55 (1966); A. Calderbank, T. E. Tomlinson, *ibid.* 252 (1968); A. Calderbank, *ibid.* **6,** 128 (1970). Toxicity studies: D. G. Clark *et al., Br. J. Ind. Med.* **23,** 126 (1966); D. M. Conning *et al., Br. Med. Bull.* **25,** 245 (1969); R. D. Kimbrough, T. B. Gaines, *Toxicol. Appl. Pharmacol.* **17,** 679 (1970); J. F. Dasta, *Am. J. Hosp. Pharm.* **35,** 1368 (1978). Controversial use on marijuana plants: R. J. Smith, *Science* **199,** 861 (1978). *Review:* A. A. Akhavein, D. L. Linscott, *Residue Rev.* **23,** 97-145 (1968); A. Calderbank, P. Slade in *Herbicides: Chemistry, Degradation and Mode of Action,* P. C. Kearney, D. Kaufman, Eds. (Dekker, New York, 2nd ed., 1976) pp 501-540.



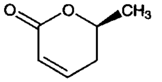
Dichloride. [1910-42-5] PP-148; Gramoxone. $C_{12}H_{14}Cl_2N_2$; mol wt 257.16. Colorless crystals, mp 300° (dec). Very sol in water, slightly sol in lower alcohols. Insol in hydrocarbons. Hydrolyzed by alkali. Inactivated by inert clays and anionic surfactants. Corrosive to metal. Non-volatile. Normal potential at 30°: −0.446 volts. LD_{50} orally in rats: 125 mg/kg (Conning).

Bismethyl sulfate. [2074-50-2] Paraquat I; PP-910. $C_{14}H_{20}N_2O_8S_2$; mol wt 408.45. Yellow solid. LD_{50} orally in male rats: 100 mg/kg (Kimbrough, Gaines).

Caution: Potential symptoms of overexposure to paraquat dichloride are irritation of eyes, skin, nose, throat, respiratory system; epistaxis; dermatitis; fingernail damage; irritation of GI tract; heart, liver, kidney damage. *See NIOSH Pocket Guide to Chemical Hazards* (DHHS/NIOSH 97-140, 1997) p 240.

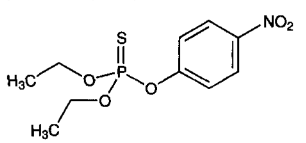
USE: Herbicide. Dichloride as biological oxidation-reduction indicator.

7032. Parasorbic Acid. [10048-32-5] (6*S*)-5,6-Dihydro-6-methyl-2*H*-pyran-2-one; 5-hydroxy-2-hexenoic acid lactone; δ-$\Delta^{\alpha,\beta}$-hexenolactone; 2-hexen-5,1-olide; sorbic oil. $C_6H_8O_2$; mol wt 112.13. C 64.27%, H 7.19%, O 28.54%. The sole constituent of "Vogelbeeröl", an oil obtained by steam distillation of the acidified juice of the ripe berries of the mountain ash, *Sorbus aucuparia* L., *Rosaceae:* Hofmann, *Ann.* **110,** 129 (1859); Doebner, *Ber.* **27,** 344 (1894); Kuhn, Jerchel, *Ber.* **76,** 413 (1943). Structure: *eidem, ibid.* Synthesis: Haynes, Jones, *J. Chem. Soc.* **1946,** 954; Lamberti *et al., Recl. Trav. Chim. Pays-Bas* **86,** 504 (1967). Pharmacology and acute toxicity: H. J. Meyer, R. Kretzschmar, *Arzneim.-Forsch.* **19,** 617 (1969).



Oily liquid, sweet aromatic odor. bp_{14} 104-105°; bp_{22} 119-123°. n_D^{25} 1.4682. d_4^{18} 1.079. $[\alpha]_D^{18}$ +49.3°; $[\alpha]_D^{19}$ +210° (c = 2 in alc). Soluble in water; freely sol in alcohol, ether. Aq solns are neutral and turn acid on storage. LD_{50} in mice (mg/kg): 420 ±6.3 i.p.; 195 ±13.6 i.v. (Meyer, Kretzschmar).

7033. Parathion. [56-38-2] Phosphorothioic acid *O,O*-diethyl *O*-(4-nitrophenyl) ester; *O,O*-diethyl *O*-*p*-nitrophenyl phosphorothioate; diethyl-*p*-nitrophenyl monothiophosphate; DNTP; S.N.P.; E-605; AC-3422; ENT-15108; Alkron; Folidol; Fostox E; Rhodiatox; Thiophos. $C_{10}H_{14}NO_5PS$; mol wt 291.26. C 41.24%, H 4.84%, N 4.81%, O 27.47%, P 10.63%, S 11.01%. Non-systemic contact and stomach insecticide and acaricide; cholinesterase inhibitor. Prepn: Thurston, *FIAT Report* **949** (1946); Coates, Topley, *BIOS Final Report* **1808** (1947). See also Fletcher *et al., J. Am. Chem. Soc.* **70,** 3943 (1948). Conversion to toxic oxygen analogs: *See* Paraoxon. Toxicity study: T. B. Gaines, *Toxicol. Appl. Pharmacol.* **14,** 515 (1969). *Review:* Hall in *Adv. Chem. Ser.* **1,** entitled "Agricultural Control Chemicals" (ACS, Washington DC, 1950) p 150. Review of industrial syntheses: Chadwick, Watt, "Thiophosphates" in *Phosphorus and Its Compounds* **vol. 2,** J. R. Van Wazer, Ed. (Interscience, New York, 1961) pp 1257-1262. Review of distribution, transport and fate in the environment: M. S. Mulla *et al., Residue Rev.* **81,** 1-159 (1981); of carcinogenic risk: *IARC Monographs* **30,** 153-181 (1983).



Pale yellow liquid. bp_{760} 375°; $bp_{0.6}$ 157-162°. mp 6°. n_D^{25} 1.5370. d_4^{25} 1.26. Vapor pressure at 20°: 3.78×10^{-5} mm Hg. Surface tension at 25°: 39.2 dynes/cm. Viscosity (25°): 15.30 cP. Absorption spectra: Williams, *Ind. Eng. Chem.* **43,** 950 (1951). Freely sol in alcohols, esters, ethers, ketones, aromatic hydrocarbons. Practically insol in water (20 ppm), petr ether, kerosene, and the usual spray oils. Incompatible with substances having a pH higher than 7.5. LD_{50} in female, male rats (mg/kg): 3.6, 13 orally; 6.8, 21 dermally (Gaines).

Caution: Potential symptoms of overexposure are miosis; rhinorrhea; headache; tight chest, wheezing, laryngeal spasm, salivation and cyanosis; anorexia, nausea, vomiting, abdominal cramps and diarrhea; sweating; muscle fasciculation, weakness and paralysis; giddiness, confusion and ataxia; convulsions, coma; low blood pressure; cardiac irregularities; skin, eye and respiratory system irritation. *See NIOSH Pocket Guide to Chemical Hazards* (DHHS/-NIOSH 97-140, 1997) p 240; *Clinical Toxicology of Commercial Products,* R. E. Gosselin *et al.,* Eds. (Williams & Wilkins, Baltimore, 5th ed., 1984) Section III, pp 336-343.

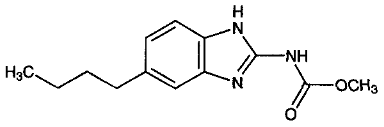
USE: Insecticide; acaricide.

7034. Parathyroid Hormone. [9002-64-6] Parathormone; PTH. Regulatory factor in the homeostatic control of calcium and phosphate metabolism, its principal sites of activity being the skeleton, kidneys, and gastrointestinal tract. Prime function is to raise plasma calcium concns. Acts synergistically with vitamin D_3, *q.v.* except in the kidneys where the latter causes phosphate retention. Secretion from the parathyroid gland varies inversely with serum Ca^{2+} concentrations, unlike calcitonin, *q.v.*, which is secreted in direct proportion to serum calcium levels. Structure consists of a single-chain polypeptide of 84 amino acid residues. Sequence varies slightly among mammalian species. Sequence of bovine PTH: Niall *et al., Z. Physiol. Chem.* **351,** 1586 (1970); Brewer, Ronan, *Proc. Natl. Acad. Sci. USA* **67,** 1862 (1970). Sequence of porcine PTH: O'Riordan *et al., Proc. R. Soc. Med.* **64,** 1263 (1971). Isoln of human PTH from parathyroid adenomas: O'Riordan *et al., Endocrinology* **89,** 234 (1971). Fragment exhibiting full biological activity consists of about 35 amino acid residues from the *N*-terminal: Potts *et al.* in *Parathyroid Hormone and Thyrocalcitonin (Calcitonin),* R. V. Talmage, L. F. Belanger, Eds. (Excerpta Medica, New York, 1968) p 44; *see* in entirety for review and special studies. Synthesis of active bovine fragment: Potts *et al., Proc. Natl. Acad. Sci. USA* **68,** 63 (1971); of human PTH (1-38): S. Funakoshi *et al., Pept. Chem.* **18,** 223 (1980). Reviews of early literature: Potts *et al., Recent Prog. Horm. Res.* **22,** 101 (1966); Arnaud *et al., Annu. Rev. Physiol.* **29,** 349 (1967). *Reviews:* Behrens, Grinnan, *Annu. Rev. Biochem.* **38,** 83 (1969); Auerbach *et al., Recent Prog. Horm. Res.* **28,** 353 (1972); Parsons, Potts, "Physiology and Chemistry of Parathyroid Hormone" in *Clinics in Endocrinology and Metabolism* I. MacIntyre, Ed. (Saunders, Philadelphia, 1972) pp 33-78. Biosynthetic review: J. F. Habener *et al., Recent Prog. Horm. Res.* **33,** 249 (1977).

Note: Aqueous solns of the active principles of bovine parathyroid gland have been used under the names: ***Parathorm, Parathor-mone, Paroidin.***

THERAP CAT: Blood calcium regulator.

7035. Parbendazole. [14255-87-9] (5-Butyl-1*H*-benzimidazol-2-yl)carbamic acid methyl ester; methyl 5-butyl-2-benzimidazolecarbamate; 5-butyl-2-(carbomethoxyamino)benzimidazole; SKF-29044; Helmatac; Verminum; Worm Guard. $C_{13}H_{17}N_3O_2$; mol wt 247.29. C 63.14%, H 6.93%, N 16.99%, O 12.94%. Prepd from 4-butyl-*o*-phenylenediamine and carbomethoxycyanamide: Actor *et al., Nature* **215,** 321 (1967); **GB 1123317** and Stedman; Actor, Pagano, **US 3480642; US 3574845** (1968, 1969, 1971 all to SKF). Activity: Ostmann, Scheidy, *Prog. Antimicrob. Anticancer Chemother., Proc. 6th Int. Congr. Chemother.* **1,** 159 (1970). Identification of metabolites: Dunn *et al., J. Med. Chem.* **16,** 996 (1973).

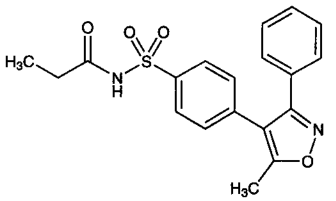


Crystals from aq ethanol, mp 225-227° (dec). uv max (95% ethanol/1*N* HCl): 282, 288 nm (ε 16200, 20000). Practically insol in water. LD_{50} in mice, rats (g/kg): >4 orally, both species (Actor).

THERAP CAT (VET): Anthelmintic.

7036. Parecoxib. [198470-84-7] *N*-[[4-(5-Methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]propanamide. $C_{19}H_{18}N_2O_4S$; mol wt 370.42. C 61.61%, H 4.90%, N 7.56%, O 17.28%, S

8.66%. Injectable prodrug of valdecoxib, *q.v.*, a selective cyclooxygenase-2 (COX-2) inhibitor. Prepn: J. J. Talley *et al.*, **WO 9738986**; *eidem*, **US 5932598** (1997, 1999 both to Searle); *eidem*, *J. Med. Chem.* **43**, 1661 (2000). Clinical pharmacokinetics: A. Karim *et al.*, *J. Clin. Pharmacol.* **41**, 1111 (2001). Pharmacological profile: S. S. V. Padi *et al.*, *Eur. J. Pharmacol.* **491**, 69 (2004). Clinical evaluation in post-surgical pain: N. A. Nussmeier *et al.*, *Anesthesiology* **104**, 518 (2006). Comparison of GI effects with ketorolac: R. R. Stoltz *et al.*, *Am. J. Gastroenterol.* **97**, 65 (2002). Review of pharmacology and clinical experience: S. M. Cheer, K. L. Goa, *Drugs* **61**, 1133-1141 (2001).



mp 148.9-151°.

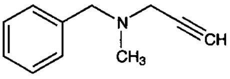
Sodium salt. [198470-85-8] SC-69124A; Dynastat. $C_{19}H_{17}N_2NaO_4S$; mol wt 392.40. mp 271.5-272.7°.

THERAP CAT: Anti-inflammatory; analgesic.

7037. Pareira. Pareira brava. Dried root of *Chondodendron platiphyllum* (A. St. Hil.) Miers, *C. microphyllum* (Eichl.) Mold., and *C. tomentosum* Ruiz et Pavon, *Menispermaceae*. *Habit.* Brazil. *Constit.* Bebeerine, chondrodine, fatty acids, tannin.

THERAP CAT: Diuretic, anti-infective (urinary).

7038. Pargyline. [555-57-7] *N*-Methyl-*N*-2-propynylbenzenemethanamine; *N*-methyl-*N*-2-propynylbenzylamine; *N*-benzyl-*N*-methyl-2-propynylamine; *N*-methyl-*N*-propargylbenzylamine; MO-911; A-19120; Eudatin; Supirdyl. $C_{11}H_{13}N$; mol wt 159.23. C 82.97%, H 8.23%, N 8.80%. Monoamine oxidase inhibitor. Prepd from propargyl bromide and benzylmethylamine: **GB 906245**; Martin, **US 3155584** (1962 and 1964, both to Abbott). Activity as a glucuronyl transferase inducer: Yeh, Mitchell, *Experientia* **28**, 298 (1972).

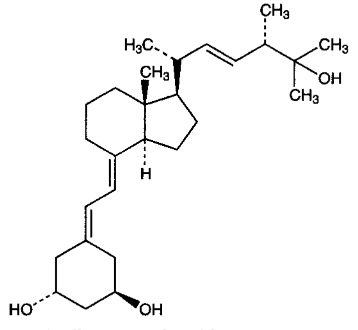


Free base, bp_{11} 96-97°.

Hydrochloride. [306-07-0] Eutonyl. $C_{11}H_{13}N.HCl$; mol wt 195.69. Crystals from ethanol + ether, mp 154-155°. Readily sol in water. Aq solns are unstable.

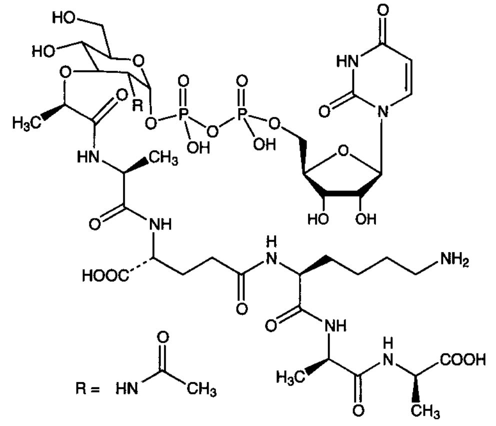
THERAP CAT: Antihypertensive.

7039. Paricalcitol. [131918-61-1] (1α,3β,7*E*,22*E*)-19-Nor-9,10-secoergosta-5,7,22-triene-1,3,25-triol; 19-nor-1α,25-dihydroxyvitamin D_2; Zemplar. $C_{27}H_{44}O_3$; mol wt 416.64. C 77.83%, H 10.64%, O 11.52%. Synthetic analog of vitamin D. Prepn: H. F. DeLuca *et al.*, **EP 387077**; *eidem*, **US 5587497** (1990, 1996 both to Wisconsin Alum. Res.). Series of articles on pharmacology and clinical experience in secondary hyperparathyroidism: *Am. J. Kidney Dis.* **32**, Suppl. 2, S40-S66 (1998). *Review:* M. M. Goldenberg, *Clin. Ther.* **21**, 432-441 (1999).



THERAP CAT: Antihyperparathyroid.

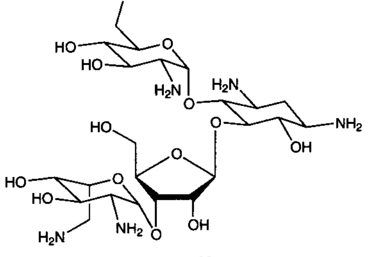
7040. Park Nucleotide. [18836-50-5] (L-lysyl form); [120010-32-4] (pimelate form). UDP-MurNAc-L-Ala-γ-D-Glu-X-D-Ala-D-Ala; stem peptide. Glyco-pentapeptide; key intermediate in bacterial cell-wall synthesis. Residue 3 varies from species to species; it is usually L-Lys in Gram positive bacteria and mesodiaminopimelate in Gram negative bacteria. Identification and isolation from *Staphylococcus aureus*: J. T. Park, *J. Biol. Chem.* **194**, 885 (1952). Total synthesis: S. A. Hitchcock *et al.*, *J. Am. Chem. Soc.* **120**, 1916 (1998); of radioiodinated analog: C. N. Eid *et al.*, *J. Labelled Compd. Radiopharm.* **41**, 705 (1998).



L-Lysyl Form

USE: Tool for antibacterial screen development.

7041. Paromomycin. [7542-37-2] *O*-2-Amino-2-deoxy-α-D-glucopyranosyl-(1 → 4)-*O*-[*O*-2,6-diamino-2,6-dideoxy-β-L-idopyranosyl-(1 → 3)-β-D-ribofuranosyl-(1 → 5)]-2-deoxy-D-streptamine; *O*-2,6-diamino-2,6-dideoxy-β-L-idopyranosyl-(1 → 3)-*O*-β-D-ribofuranosyl-(1 → 5)-*O*-[2-amino-2-deoxy-α-D-glucopyranosyl-(1 → 4)]-2-deoxystreptamine; paromomycin I; amminosidin; catenulin; crestomycin; estomycin; hydroxymycin; monomycin A; neomycin E; paucimycin; R-400. $C_{23}H_{45}N_5O_{14}$; mol wt 615.63. C 44.87%, H 7.37%, N 11.38%, O 36.38%. Oligosaccharide-type antibiotic isolated from various *Streptomyces*. From *S. rimosus* forma *paromomycinus:* Frohardt *et al.*, **US 2916485** (1959 to Parke, Davis); from *S. catenulae:* Davisson, Finlay, **US 2895876** (1959 to Pfizer); from *S. chrestomyceticus:* Canevazzi, Scotti, *G. Microbiol.* **7**, 242 (1959); Arcamone *et al.*, *ibid.* 251. Identity of paromomycin, catenulin, hydroxymycin and aminosidine: Schillings, Schaffner, *Antimicrob. Agents Chemother.* **1961,** 274. Structure: Haskell *et al.*, *J. Am. Chem. Soc.* **81**, 3480, 3482 (1959); Rinehart *et al.*, *ibid.* **84**, 3218 (1962); Hichens, Rinehart, ibid. **85**, 1547 (1963). Probable identity with ***zygomycin A***: Horii, *J. Antibiot.* **15A**, 187 (1962). Identity with monomycin A: Konstantinova, Brazhnikova, *Antibiotiki* **10**(1), 34 (1965); with neomycin E: Hessler *et al.*, *J. Antibiot.* **23**, 464 (1970). Toxicity data: A. DiMarco, C. Bertazzoli, *Antibiot. Chemother.* **11**, 2 (1963). Review of antimicrobial activity: G. L. Coffey *et al.*, *ibid.* **9**, 730 (1959). Review of pharmacology: Gasparini, Pignatelli, *Veterinaria (Milan)* **21**, 7 (1972).



Amorphous white powder. $[\alpha]_D^{25}$ +65 ±3°. Soluble in water; moderately sol in methanol; sparingly sol in abs ethanol. LD_{50} in rats, mice (mg/kg): >1625, >2275 orally; >650, 423 s.c.; 156, 90 i.v. (Coffey).

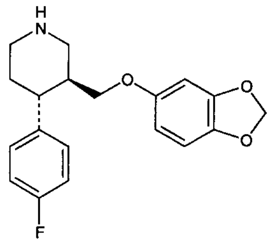
Sulfate. [1263-89-4] 1600 Antibiotic; FI-5853; Aminoxidin; Aminosidine; Farmiglucin; Farminosidin; Gabbromicina; Gabbromycin; Gabbroral; Humagel; Humatin; Pargonyl; Paramicina; Paricina; Sinosid. $C_{23}H_{45}N_5O_{14}.H_2SO_4$; mol wt 713.71. $[\alpha]^{25}_D$ +50.5° (c = 1.5 in water pH 6). LD_{50} in mice (mg/kg): ~15,000 orally; 700 s.c.; 110 i.v. (Di Marco, Bertazzoli).

THERAP CAT: Antibacterial; antiamebic.

THERAP CAT (VET): Antiamebic.

7042. Parotin. [1392-81-0] Salivary gland hormone; protein of globulin nature having an isoelectric point of pH 5.7. Produced by the parotid gland. Structure studies: Ito *et al., Endocrinol. Jpn.* **12,** 249 (1966); Shimasaki *et al., ibid.* **14,** 11 (1967). Generally acts on the mesenchymal tissues, esp the hard and connective tissues, to promote their development and growth. Also has a protein-anabolic function. Hypocalcemic and leukocytosis-promoting activities: Ito *et al., ibid.* **12,** 298 (1966). *Reviews:* Yosoji Ito, *J. Jpn. Biochem. Soc.* **25,** 143-164 (1953); *Ann. N.Y. Acad. Sci.* **85,** art. 1, 228-310 (1960).

7043. Paroxetine. [61869-08-7] (3*S-trans*)-3-[(1,3-Benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)piperidine; (−)-*trans*-4-(*p*-fluorophenyl)-3-[[3,4-(methylenedioxy)phenoxy]methyl]piperidine; FG-7051; BRL-29060. $C_{19}H_{20}FNO_3$; mol wt 329.37. C 69.28%, H 6.12%, F 5.77%, N 4.25%, O 14.57%. Selective serotonin (5-HT) reuptake inhibitor (SSRI). Prepn: J. A. Christensen, R. F. Squires, **DE 2404113**; *eidem,* **US 3912743**; **US 4007196** (1974, 1975, 1977 all to Ferrosan); of crystalline hydrochloride hemihydrate: R. D. B. Barnes *et al.,* **EP 223403**; **US 4721723** (1987, 1988 both to Beecham). Characterization of serotonin inhibition: J. Buus Lassen, *Eur. J. Pharmacol.* **47,** 351 (1978). Binding to serotonin transporter complex: E. Habert *et al., ibid.* **118,** 107 (1985). Clinical pharmacokinetics: J. Lund *et al., Acta Pharmacol. Toxicol.* **51,** 351 (1982). HPLC determn in plasma: M. A. Brett *et al., J. Chromatogr.* **419,** 438 (1987). Clinical trial in obsessive-compulsive disorder: J. Zohar *et al., Br. J. Psychiatry* **169,** 468 (1996); in social phobia: M. B. Stein *et al., J. Am. Med. Assoc.* **280,** 708 (1998). Review of pharmacology and clinical use in depression: K. L. Dechant, S. P. Clissold, *Drugs* **41,** 225-253 (1991); of clinical experience: D. Dunner, R. Kumar, *Pharmacopsychiatry* **31,** 89-101 (1998); of use in generalized social anxiety disorder: M. Van Ameringen *et al., Expert Opin. Pharmacother.* **6,** 819-830 (2005).

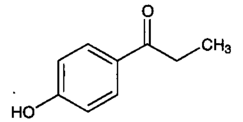


Hydrochloride hemihydrate. [110429-35-1]; [78246-49-8] (hydrochloride). Aropax; Deroxat; Paxil; Seroxat. $C_{19}H_{20}FNO_3.HCl.½H_2O$; mol wt 374.83. Crystals, mp 129-131°. Soly in water: 5.4 mg/ml.

Maleate. [64006-44-6] Crystals from ethanol-ether, mp 136-138°. $[\alpha]_D$ −87° (c = 5 in ethanol). LD_{50} in mice (mg/kg): 845 s.c.; 500 orally (Christensen, Squires, 1977).

THERAP CAT: Antidepressant; antiobsessional.

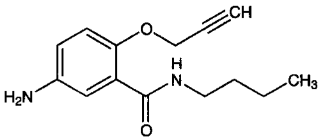
7044. Paroxypropione. [70-70-2] 1-(4-Hydroxyphenyl)-1-propanone; 4′-hydroxypropiophenone; *p*-hydroxypropiophenone; paraoxypropiophenone; *p*-propionylphenol; ethyl *p*-hydroxyphenyl ketone; P.O.P.; B-360; H-365; Profenone; Frenantol; Frenohypon; Paroxon; Possipione; Hypostat. $C_9H_{10}O_2$; mol wt 150.17. C 71.98%, H 6.71%, O 21.31%. Prepn: Perkin, *J. Chem. Soc.* **55,** 546 (1889); Goldzweig, Kaiser, *J. Prakt. Chem.* [2] **43,** 86 (1891); Cox, *J. Am. Chem. Soc.* **49,** 1028 (1927); Hartung *et al., ibid.* **53,** 4153 (1931); Farinholt, *ibid.* **55,** 3386 (1933); Miller, Hartung, *Org. Synth.* **coll. vol. II** (1943) p 543. Derivatives: Buu-Hoi, *Rec. Trav. Chim.* **68,** 759 (1949).



Needles or prisms from water. mp 149°. One part dissolves in 2896 parts of water at 15°, in 30 parts at 100°. Freely sol in alcohol or ether.

THERAP CAT: Pituitary gonadotropic hormone inhibitor.

7045. Parsalmide. [30653-83-9] 5-Amino-*N*-butyl-2-(2-propynyloxy)benzamide; 5-amino-*O*-propynyl-*N*-butylsalicylamide; 2-propargyloxy-5-amino-*N*-butylbenzamide; MY-41-6; Sinovial; Parsal. $C_{14}H_{18}N_2O_2$; mol wt 246.30. C 68.27%, H 7.37%, N 11.37%, O 12.99%. Prepn: B. Gradnik *et al.,* **DE 2029991**; *eidem,* **US 3739030** (1970, 1973 both to Soc. Etude Recher. Sci. Med.). Synthesis and pharmacology: A. Pedrazzoli *et al., Boll. Chim. Farm.* **115,** 125 (1976). Effect on gastric secretion in laboratory animals: G. Bertaccini *et al., Farmaco Ed. Prat.* **34,** 482 (1979). Inhibition of platelet aggregation: R. Fantasia *et al., Arzneim.-Forsch.* **32,** 1312 (1982). Clinical comparison with phenylbutazone, *q.v.,* in management of joint pain: A. Bajardi, S. Fantato, *Minerva Med.* **67,** 3371 (1976); S. Menci *et al., ibid.* 3403. Series of articles on anti-inflammatory activity, pharmacology and toxicology: *Boll. Chim. Farm.* **115,** 135-230 (1976), *C.A.* **85,** 13981-13986 (1976).



Crystals from ethanol, mp 83-85°. pKa (aq soln, 20°) 4.6 ±0.03. uv max (abs alcohol): 220 ±1, 327 ±2 nm; (water, pH 2): 284 nm (log ε 3.39); (water, pH 8.5): 313 nm (log ε 3.40). Very soluble in alcohol, chloroform, acetone, ethyl acetate, dioxane; slightly sol in water. Practically insol in petr ether, cyclohexane.

THERAP CAT: Anti-inflammatory; analgesic.

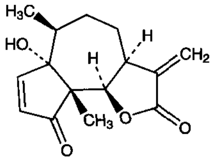
7046. Parsley. Biennial herb, *Petroselinum crispum* (Mill.) Nyman, *Umbelliferae*; also known as *P. sativum* Hoffm. *Habit.* Mediterranean region; cultivated worldwide. *Constit.* Flavonoids, esp. apiin, luteolin; furocoumarins, incl. bergapten (0.02%), oxypeucedanin (0.01%); volatile oils (0.05% in leaf, 2-7% in seed); fixed oil, protein, carbohydrate, vitamins, esp. A and C. GC-MS determn of volatile components: M. G. López *et al., J. Agric. Food Chem.* **47,** 3292 (1999). Comprehensive description and medicinal uses: J. Barnes *et al., Herbal Medicines* (Pharmaceutical Press, London, 2nd Ed., 2002) pp 365-367.

Parsley seed oil. [8000-68-8] Obtained by steam distillation of the ripe seed. *Constit.* Apiole, myristicin, tetramethoxyallylbenzene. Review of toxicology: *Food Cosmet. Toxicol.* **15,** 897-898 (1975). Yellow to light brown liquid with herbal-like odor. d^{25}_{25} 1.040-1.080. n^{20}_D 1.513-1.522. Saponification value between 2 and 10. Acid value not more than 4.0. Very slightly sol in water; slightly sol in propylene glycol; sol in 6 vols 80% alcohol. Insol in glycerin.

USE: Flavoring in foods and pharmaceuticals.

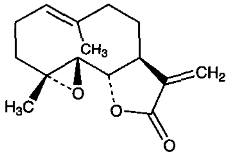
THERAP CAT: In treatment of urinary tract inflammation and kidney stones; carminative.

7047. Parthenin. [508-59-8] [3a*S*-(3aα,6β,6aα,9aβ,9bα)]-3,3a,4,5,6,6a,9a,9b-Octahydro-6a-hydroxy-6,9a-dimethyl-3-methyleneazuleno[4,5-*b*]furan-2,9-dione; 1,6β-dihydroxy-4-oxo-10α*H*-ambrosa-2,11(13)-dien-12-oic acid γ-lactone; parthenicin. $C_{15}H_{18}O_4$; mol wt 262.30. C 68.68%, H 6.92%, O 24.40%. From herb of *Parthenium hysterophorus* L., *Compositae.* Parthenin is the substance largely responsible for the allergic contact dermatitis caused by *P. hysterophorus.* Isoln: Arny, *Am. J. Pharm.* **69,** 169 (1897). Isoln and structure: Herz *et al., Tetrahedron Lett.* **1961,** 82; Herz *et al., J. Am. Chem. Soc.* **84,** 2601 (1962). Abs config: Emerson *et al., Tetrahedron Lett.* **1966,** 6151. Total synthesis of (±)-form: P. Kok *et al.*, *Bull. Soc. Chim. Belg.* **87,** 615 (1978); C. H. Heathcock *et al.*, *J. Am. Chem. Soc.* **104,** 6081 (1982).



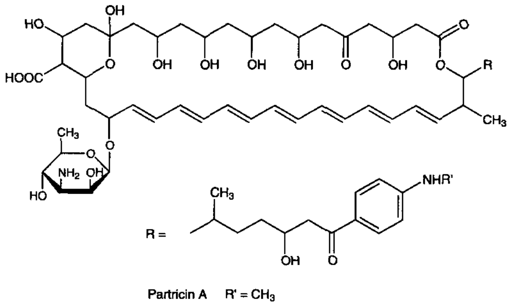
Crystals from water, mp 163-166°. $[\alpha]_D^{25}$ +7.02° (c = 2.71 in chloroform). uv max: 215, 340 nm (ε 15,100; 22). Practically insol in water. Sol in alcohol, chloroform, ether, ethyl acetate.

7048. Parthenolide. [20554-84-1] (1a*R*,4*E*,7a*S*,10a*S*,10b*S*)-2,3,6,7,7a,8,10a,10b-Octahydro-1a,5-dimethyl-8-methyleneoxireno[9,10]cyclodeca[1,2-*b*]furan-9(1a*H*)-one; 4,5α-epoxy-6β-hydroxy-germacra-1(10),11(13)-dien-12-oic acid γ-lactone. $C_{15}H_{20}O_3$; mol wt 248.32. C 72.55%, H 8.12%, O 19.33%. Sesquiterpene lactone found in feverfew, *q.v.*, and in other plants. Isolation from *Chrysanthemum parthenium* (L.) Bernh. *Compositae* and characterization: V. Herout *et al.*, *Chem. Ind. (London)* **1959,** 1069; M. Soucek *et al.*, *Collect. Czech. Chem. Commun.* **26,** 803 (1961); from *Magnolia grandiflora* L., *Magnoliaceae:* F. S. El-Feraly, Y.-M. Chan, *J. Pharm. Sci.* **67,** 347 (1978). Revised structure and spectral analysis: T. R. Govindachari *et al.*, *Tetrahedron* **21,** 1509 (1965). Absolute configuration: A. S. Bawdekar *et al.*, *Tetrahedron Lett.* **1966,** 1225. Crystal structure: A. Quick, D. Rogers, *J. Chem. Soc. Perkin Trans. 2* **4,** 465 (1976). HPLC determn: D. Strack *et al.*, *Z. Naturforsch.* **35,** 915 (1980). Cytotoxicity: K.-H. Lee *et al.*, *Cancer Res.* **31,** 1649 (1971); L. A. J. O'Neill *et al.*, *Br. J. Clin. Pharmacol.* **23,** 81 (1987).



Colorless plates, mp 115-116°. $[\alpha]_D^{20}$ −81.4° (c = 1.04 in chloroform); $[\alpha]_D^{22}$ −71.4° (c = 0.220 in CH_2Cl_2). uv max: 214 nm (log ε 4.22).

7049. Partricin. [11096-49-4] Ayfactin; SPA-S-132; Heptaene macrolide antibiotic complex produced by *Streptomyces aureofaciens* NRRL 3878. Isoln: T. Bruzzese, R. Ferrari, **US 3773925** (1973 to SPA). Recovery and purification process: S. Magnaghi *et al.*, **GB 1462442** (1977 to SPA), *C.A.* **87,** 66588a (1977). *In vitro* activity: W. Ritzerfeld, *Farmaco Ed. Sci.* **27,** 235 (1972); G. A. Meloni *et al.*, *ibid.* **34,** 183 (1979). Use in treatment of benign prostatic hypertrophy: T. Bruzzese, L. Ferrari, **US 4237117** (1980 to SPA). Separation, characterization and structure of components A and B: R. C. Tweit *et al.*, *J. Antibiot.* **35,** 997 (1982).



Partricin A R' = CH3
Partricin B R' = H

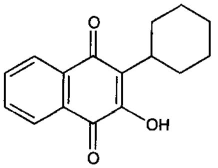
Partricin A. $C_{59}H_{86}N_2O_{19}.4H_2O$; mol wt 1199.38. Greenish-yellow powder, mp >300° (dec). uv max (75% methanol in DMF): 232, 240, 247, 288, 342, 358, 378, 400 nm (ε 33476, 32237, 22936, 15493, 58282, 76883, 102308, 89280). pKa's (70% aq DMF): 6.07, 8.91.

Partricin B. $C_{58}H_{84}N_2O_{19}.2\frac{1}{2}H_2O$; mol wt 1158.33. Brownish-yellow powder, mp >300° (dec). uv max (75% methanol in DMF): 232, 240, 247, 288, 342, 358, 378, 400 nm (ε 34761, 32826, 23174, 20594, 50207, 73392, 100425, 87558). pKa's (70% aq DMF): 6.31, 8.95. $[\alpha]_D^{26}$ +87.2° (c = 0.06 in DMF).

Complex. Amphoteric yellow crystals. uv max (ethanol): 401, 379, 359, 341 nm. Sol in DMF, DMSO, dimethyl acetamide, pyridine. Practically insol in water, common organic solvents. LD_{50} in mice (mg/kg): 300 orally; 0.5 i.p. (Bruzzese).

Methyl ester *see* Mepartricin.

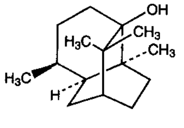
7050. Parvaquone. [4042-30-2] 2-Cyclohexyl-3-hydroxy-1,4-naphthalenedione; 2-cyclohexyl-3-hydroxy-1,4-naphthoquinone; 2-hydroxy-3-cyclohexyl-1,4-naphthoquinone; BW-993C; Clexon. $C_{16}H_{16}O_3$; mol wt 256.30. C 74.98%, H 6.29%, O 18.73%. Prepn: L. F. Fieser, *J. Am. Chem. Soc.* **70,** 3165 (1948); L. F. Fieser, M. T. Leffler, **US 2553648** (1951 to Research Corp.). Antimalarial activity: L. F. Fieser, A. P. Richardson, *J. Am. Chem. Soc.* **70,** 3156 (1948). Electron transport inhibition: A. L. Tappel, *Biochem. Pharmacol.* **3,** 289 (1960); by uncoupling: J. L. Howland, *Biochim. Biophys. Acta* **131,** 247 (1967). *In vitro* and *in vivo* antiprotozoal activity: A. T. Hudson *et al.*, *Parasitology* **90,** 45 (1985). Bioassay in serum: N. McHardy, J. Mercer, *Kenya Vet.* **8**(2), 9 (1984). Treatment of East Coast fever in cattle: T. T. Dolan *et al.*, *Vet. Parasitol.* **15,** 103 (1984); of *Theileria annulata* in calves: N. McHardy, D. W. Morgan, *Res. Vet. Sci.* **39,** 1 (1985). Field comparison of antitheilarial activity with buparvaquone, *q.v.:* N. McHardy *et al.*, *ibid.* 39.



Bright yellow needles, mp 135-136°.
THERAP CAT (VET): Antiprotozoal (Theileria).

7051. Passiflora. Passion flower; passion vine; May pops. Dried flowering and fruiting tops of *Passiflora incarnata* L., *Passifloraceae. Habit.* Southeastern U.S. *Constit.* Harman.
THERAP CAT: Sedative, analgesic.

7052. Patchouli Alcohol. [5986-55-0] [1*R*-(1α,4β,4aα,6β,8aα)]-Octahydro-4,8a,9,9-tetramethyl-1,6-methanonaphthalen-1(2*H*)-ol; patchouli camphor. $C_{15}H_{26}O$; mol wt 222.37. C 81.02%, H 11.79%, O 7.19%. A tricyclic sesquiterpene alcohol isolated from oil of patchouli: Gadamer, Amenomiya, *Arch. Pharm.* **241,** 39 (1903). Proposed structure: Treibs, *Ann.* **564,** 141 (1949). Revised structure: Dobler *et al.*, *Proc. Chem. Soc. London* **1963,** 383. Structural studies: Büchi *et al.*, *J. Am. Chem. Soc.* **78,** 1262 (1956); **83,** 927 (1961); **84,** 3205 (1962); **86,** 4438 (1964). Synthesis of *dl*-form: Danishevsky, Dumas, *Chem. Commun.* **1968,** 1287; Mirrington, Schmalzl, *J. Org. Chem.* **37,** 2871 (1972); K. Yamada *et al.*, *Tetrahedron* **35,** 293 (1979). Stereoselective total synthesis of racemic form: F. Näf, G. Ohloff, *Helv. Chim. Acta* **57,** 1868 (1974); of natural, racemic and (+)-forms: F. Näf *et al.*, *ibid.* **64,** 1387 (1981). *Review:* Walker, *Manuf. Chem. Aerosol News* **39,** no. 7, 27 (1968).



Large crystals (hexagonal-trapezohedral) from the higher boiling fractions of oil of patchouli or from petr ether, mp 56°. mp (racemate) 39-40° (Danishevsky, Dumas); also reported as mp 46-47° (Mirrington, Schmalzl). bp_8 140°. d_4^{20} 1.0284. $[\alpha]_D^{20}$ −97.4° (c = 24 in chloroform). n_D^{65} 1.5029. Practically insol in water. Sol in alcohol, ether, common organic solvents.