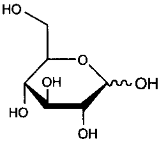
Percival, *Structural Carbohydrate Chemistry* (J. Garnet Miller, London, 1962) pp 51-57. Comprehensive monograph: H. Bartelheimer *et al.*, *D-Glucose und verwandte Verbindungen in Medizin und Biologie* (Enke, Stuttgart, 1966) 1126 pp.



α-Form monohydrate. Crystals from water, mp 83°. $[\alpha]_D$ +102.0° ⟶ +47.9° (water). 0.74 times as sweet as sucrose. One gram dissolves in about 1 ml water and in about 60 ml alcohol.

α-Form anhydr. Crystals from hot ethanol or water, mp 146°. $[\alpha]_D$ +112.2° ⟶ +52.7° (c = 10 in water). The final value is obtained instantly in the presence of hydroxyl ions. Formula for varying concns: $[\alpha]_D^{20}$ +52.5° + 0.0188p (p = g/100 ml). pH of 0.5 molar aq soln 5.9. $d_{17.5}^{17.5}$ of water solns w/v: 5% = 1.019; 10% = 1.038; 20% = 1.076; 30% = 1.113; 40% = 1.149. n_D^{20} 10% soln 1.3479. One gram dissolves in 1.1 ml water at 25°; in 0.8 ml at 30°; in 0.41 ml at 50°; in 0.28 ml at 70°; in 0.18 ml at 90°; in 120 ml methanol at 20°. Very sparingly sol in abs alcohol, ether, acetone; sol in hot glacial acetic acid, pyridine, aniline.

β-Form. Crystals from hot water + ethanol, from dil acetic acid, or from pyridine, mp 148-155°. $[\alpha]_D$ +18.7° ⟶ +52.7° (c = 10 in water).

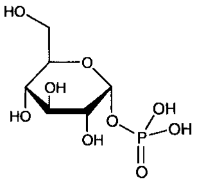
THERAP CAT: Antihypoglycemic; fluid and nutrient replenisher.
THERAP CAT (VET): Antihypoglycemic; fluid and nutrient replenisher.

4460. Glucose Oxidase. [9001-37-0] β-D-Glucopyranose aerodehydrogenase; P-FAD; corylophyline; microcide; mikrotsid; notatin. An enzyme obtained from mycelia of fungi, such as *Aspergilli* and *Penicillia;* a typical aerobic dehydrogenase which catalyzes the oxidation of glucose to gluconic acid (molecular oxygen is reduced to hydrogen peroxide). It is a flavoprotein, the prosthetic group being flavine-adenine dinucleotide (FAD). Commercial prepns frequently contain appreciable amounts of another enzyme, catalase, which is desirable for certain uses since it removes hydrogen peroxide aerobically generated by glucose oxidase. Names of some commercial prepns are: ***DeeO***, ***Fermcozyme***, ***OxyBan***, ***Ovazyme***. Isoln from *Penicillia* cultures: Coulthard *et al.*, *Biochem. J.* **39,** 24 (1945). Commercial production from *Aspergilli* and *Penicillia:* Goldsmith *et al.*, **US 2926122** (1960); from *Aspergillus niger:* Faucett *et al.*, **US 3102081** (1963 to Miles Labs.). Removal of proteolytic enzymes from glucose oxidase (contg catalase) obtained from *Aspergilli* or *Penicillia* cultures: Ohlmeyer, **US 2940904** (1960 to Ben L. Sarett). Separation from catalase: Pazur *et al.*, *Biochim. Biophys. Acta* **65,** 369 (1962). Properties: Muller, *Enzymologia* **10,** 40 (1941); Keilin, Hartree, *Biochem. J.* **42,** 221 (1948), **50,** 331 (1952). *Reviews:* L. A. Underkofler "Glucose Oxidase: Production, Properties, Present and Potential Applications" in *Soc. Chem. Ind. (London) Monograph* **no. 11,** 72-86 (1961); R. Bentley, "Glucose Oxidase" in *The Enzymes* **vol. 7,** P. D. Boyer *et al.*, Eds. (Academic Press, New York, 1963) pp 567-586. Review of use as analytical reagent: J. Raba, H. A. Mottola, *Crit. Rev. Anal. Chem.* **25,** 1-42 (1995).

Amorphous powder or crystals. Abs max between 270-280, 375-380, and 450-460 nm (aq soln). Freely sol in water giving yellowish-green solns. Most active at pH 5.5-6.0 and 30-35°. Stable between pH 4.5 and 7.0. Stable to pepsin and trypsin. A glucose oxidase unit is defined as that quantity of enzyme which will cause the uptake of 10 mm^3 oxygen per min in a Warburg manometer at 30° in the presence of excess air and excess catalase with a substrate contg 3.3% glucose monohydrate and 0.1*M* phosphate buffer, pH 5.9 with 0.4% sodium dehydroacetate: Scott, *J. Agric. Food Chem.* **1,** 727 (1953).

USE: Analytical reagent for the selective determn of glucose. Food additive for the removal of glucose during the prepn of dried egg products. Antioxidant in food and food wrappers. Stabilizer for ascorbic acid and vitamin B_{12}.

4461. α-Glucose-1-phosphate. [59-56-3] α-D-Glucopyranose 1-dihydrogenphosphate; α-glucose-1-phosphoric acid; α-D-glucopyranose-1-phosphate; Cori ester. $C_6H_{13}O_9P$; mol wt 260.14. C 27.70%, H 5.04%, O 55.35%, P 11.91%. Found widely in both plants and animals. In plants it is the immediate precursor of starch, and in animals of glycogen, being also the first product in the breakdown and utilization of these substances. Isoln from muscle and synthesis using trisilver phosphate: Cori *et al.*, *J. Biol. Chem.* **121,** 465 (1937); Krahl, Cori, *Biochem. Prep.* **1,** 33 (1949). Prepn from α-acetobromglucose + silver diphenyl phosphate: Posternak, *J. Am. Chem. Soc.* **72,** 4824 (1950); by phosphorolysis of starch using phosphorylase and orthophosphate: McCready, Hassid, *Biochem. Prep.* **4,** 63 (1955). Structure: Wolfrom, Pletcher, *J. Am. Chem. Soc.* **63,** 1050 (1941). Configuration: Wolfrom *et al.*, *ibid.* **64,** 23 (1942); Harmon, *Diss. Abstr.* **24,** 4400 (1964); Beevers, Maconochie, *Acta Crystallogr.* **18,** 232 (1965).



Free acid. $[\alpha]_D^{25}$ +120°. pK_1 = 1.11; pK_2 = 6.13. Stronger acid than H_3PO_4. Extremely sol in water.

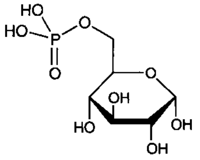
Barium salt trihydrate. [6056-70-8] Nonhygroscopic, stable powder. $[\alpha]_D^{25}$ +75° (c = 1.26). Easily sol in water.

Calcium salt. [119119-85-6] Actigam.

Dipotassium salt dihydrate. [5996-14-5] Crystals from ethanol. $[\alpha]_D^{20}$ +78° (c = 4); $[\alpha]_{549}^{20}$ +90° (c = 4). Freely sol in water.

THERAP CAT: Calcium salt as roborant.

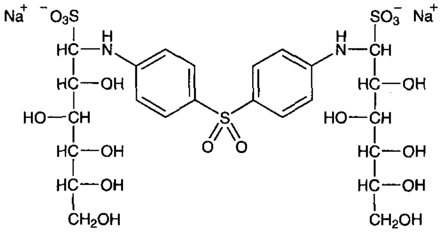
4462. Glucose-6-phosphate. [56-73-5] D-Glucose 6-(dihydrogen phosphate); glucose-6-phosphoric acid; Robison ester. $C_6H_{13}O_9P$; mol wt 260.14. C 27.70%, H 5.04%, O 55.35%, P 11.91%. A normal constituent of resting muscle, probably always existing in equilibrium with fructose-6-phosphate. For the enzymatic conversion from the 1-phosphate *see* α-Glucose-1-phosphate. Isoln from a crude mixture of hexose phosphates, obtained by yeast fermentation: Robison, King, *Biochem. J.* **25,** 323 (1931). Prepn by the action of phosphoglucomutase on α-glucose-1-phosphate: Colowick, Sutherland, *J. Biol. Chem.* **144,** 423 (1942); from acetone glucose: Levene, Raymond, *ibid.* **92,** 757 (1931); by phosphorylation of 1,2,3,4-tetraacetylglucose followed by deacetylation: Fischer, Lardy, *ibid.* **164,** 513 (1946); *Biochem. Prep.* **2,** 39 (1952). Prepn from starch: de Chatelperron *et al.*, **FR 1379068** (1964), *C.A.* **62,** 9394b (1965).



Barium salt. $C_6H_{11}O_5PO_4Ba$. Nonhygroscopic, stable powder. $[\alpha]_D^{24}$ +17.9°. Easily sol in water.

Dipotassium salt. $C_6H_{11}O_5PO_4K_2$. Precipitate from methanol. $[\alpha]_D^{24}$ +21.2° (c = 1.3). Freely sol in water.

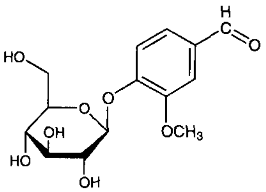
4463. Glucosulfone Sodium. [554-18-7] 1,1′-[Sulfonylbis(4,1-phenyleneimino)]bis[1-deoxy-1-sulfo-D-glucitol] disodium salt; *p,p′*-sulfonyldianiline *N,N′*-diglucoside disodium disulfonate; *p,p′*-sulfonyldianiline-*N,N′*-di-D-glucose sodium bisulfite compd; *p,p′*-diaminodiphenylsulfone-*N,N′*-di(dextrose sodium sulfonate); disodium *p,p′*-diaminodiphenylsulfone-*N,N′*-diglucose sulfonate; 501-P; Protomin; Promin; Promanide. $C_{24}H_{34}N_2Na_2O_{18}S_3$; mol wt 780.70. C 36.92%, H 4.39%, N 3.59%, Na 5.89%, O 36.89%, S 12.32%. Prepd by refluxing a mixture of 4,4′-diaminodiphenylsulfone, glucose, sodium bisulfite, and 80% ethanol: **CH 234108** (1944 to B. Siegfried), *C.A.* **43,** 4297a (1949); B. C. Jain *et al.*, *Sci. Cult.* **11,** 568 (1946). Structure activity study: W. Logemann, G. P. Miori, *Arzneim.-Forsch.* **5,** 213 (1955). Clinical evaluation in ocular leprosy: A. Bouzas, *Arch. Ophthalmol.* **31,** 629 (1971).



White, amorphous powder. Soluble in water; slightly sol in ethanol. Insol in ether, benzene, methanol, ethyl acetate, pyridine. Aq solns may be sterilized by autoclaving. LD_{50} in rats (g/kg): 3-4 orally, 3-3.5 i.v. (Logemann, Miori).

THERAP CAT: Antibacterial (leprostatic).

4464. Glucovanillin. [494-08-6] 4-(β-D-Glucopyranosyloxy)-3-methoxybenzaldehyde; vanillin-D-glucoside; avenein; vanilloside. $C_{14}H_{18}O_8$; mol wt 314.29. C 53.50%, H 5.77%, O 40.73%. From green fruit of vanilla: Goris, *Compt. Rend.* **179,** 70 (1924). From coniferin by oxidation with CrO_3: Tremann, *Ber.* **18,** 1595 (1885). Structure and synthesis: Fischer, Raske, *Ber.* **42,** 1475 (1909); Thorpe, Williams, *J. Chem. Soc.* **1937,** 494.

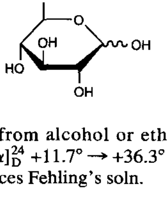


Needles from methanol, mp 189-190°. Bitter taste. $[\alpha]_D^{20}$ −89.9° (water). Soluble in hot water, alcohol. Almost insol in ether.

Tetraacetate. $C_{22}H_{26}O_{12}$. Crystals from dil alcohol, mp 142-143°. $[\alpha]_D$ −48.3° (chloroform).

USE: Pharmaceutic aid (flavor).

4465. D-Glucuronic Acid. [6556-12-3] $C_6H_{10}O_7$; mol wt 194.14. C 37.12%, H 5.19%, O 57.69%. Widely distributed in the plant and animal kingdoms. Usually occurs in "paired" form, *i.e.* as a glycosidic combination with phenols, alcohols, etc. Such glucuronides form in the liver to detoxify poisonous hydroxyl-containing substances. The glucuronides present in normal urine are those of phenol, cresol, and indoxyl. After the ingestion of poisons such as morphine, chloral hydrate, camphor, or turpentine, glucuronides formed with the poison or its hydroxylated derivatives appear in the urine. Review and bibliography: Stacey, *Adv. Carbohydr. Chem.* **2,** 161 (1946); Jones, Smith, *ibid.* **4,** 243 (1949). Structure: Pryde, Williams, *Nature* **128,** 187 (1931); Levene, Meyer, *J. Biol. Chem.* **92,** 257 (1931); Levene, Kreider, *ibid.* **120,** 597 (1937). Review of syntheses: Mehltretter, *Adv. Carbohydr. Chem.* **8,** 231 (1953). Prepn by irradiation of D-glucose in dil aq soln: Phillips *et al., J. Chem. Soc.* **1958,** 3522; by γ-irradiation of aq sucrose soln: Phillips, Moody, *ibid.* **1960,** 762. Electrophoretic sepn of D-glucuronic acid and its C-5 epimer, ***L-iduronic acid***: I. Miyamoto, S. Nagase, *Anal. Biochem.* **115,** 308 (1981). Monographs: N. E. Artz, E. M. Osman, *Biochemistry of Glucuronic Acid* (Academic Press, New York, 1950); G. J. Dutton, Ed., *Glucuronic Acid, Free and Combined* (Academic Press, New York, 1966) 629 pp.



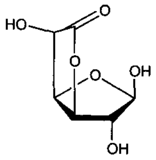
β-Form. Needles from alcohol or ethyl acetate. mp 165°. Shows mutarotation: $[\alpha]_D^{24}$ +11.7° → +36.3° (2 hrs, c = 6). Soluble in water, alcohol. Reduces Fehling's soln.

4466. β-Glucuronidase. [9001-45-0] Glusulase. Glucuronide-splitting enzyme found in liver, spleen, and certain tissues of the endocrine and reproductive systems. Rats seem to have a higher concn than other mammals. Also found in fish liver, snails, mollusks, and some insects. Isoln from rat livers, kidneys, and spleens: Fishman, Talalay, *Science* **105,** 131 (1947). *Review and bibliography:* Fishman, *Adv. Enzymol.* **16,** 361-409 (1955).

White powder. Soluble in water.

USE: In the determination of urinary steroids and of steroid conjugates in blood.

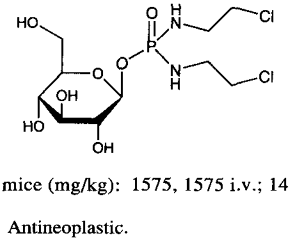
4467. D-Glucuronolactone. [32449-92-6] D-Glucuronic acid γ-lactone; D-glucofuranurono-6,3-lactone; glucurolactone; glucurone; Dicurone; Glucoxy; Guronsan. $C_6H_8O_6$; mol wt 176.12. C 40.92%, H 4.58%, O 54.51%. Found in many plant gums in polymeric combination with other carbohydrates. Important structural constituent of practically all fibrous and connective tissues in the animal organism, *cf.* D-glucuronic acid. Prepd synthetically from many polysaccharides or suitable glucosides where the hydroxyl at carbon 6 may be oxidized while the other sensitive groups are protected. Prepn: Stacey, *J. Chem. Soc.* **1939,** 1529; Hardegger, Spitz, *Helv. Chim. Acta* **33,** 337 (1950); Marsh, *Proc. Biochem. Soc.* [*Biochem. J.*], **50,** XI (1951); Mehltretter *et al., J. Am. Chem. Soc.* **73,** 2424 (1951); Phillips, Moody, *J. Chem. Soc.* **1960,** 762. Structure: J. Stanek *et al., The Monosaccharides* (Academic Press, New York, 1963) p 259. For isoln procedures see the ref under glucuronic acid.



Crystals from ethanol, mp 176-178°. (Commercial grades, mp 172°.) d_4^{30} 1.76. $[\alpha]_D^{25}$ +19.8° (c = 5.19). Soluble in water (26.9 g/100 ml of soln); slightly sol in methanol (2.8 g/100 ml). Very slightly sol in abs ethanol (0.7 g/100 ml), in glacial acetic acid (0.3 g/100 ml). The free acid is more sol than the lactone. At room temp an aq soln of glucuronolactone reaches an equilibrium of about 20% lactone and 80% acid within 2 months. At 100° an equilibrium of 60% lactone and 40% free acid is reached within 2 hrs. Initial pH of 10% aq soln 3.5, after 1 week the pH is about 2.5.

THERAP CAT: Detoxicant.

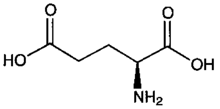
4468. Glufosfamide. [132682-98-5] 1-[*N,N'*-Bis(2-chloroethyl)phosphorodiamidate]-β-D-glucopyranose; β-D-glucopyranosyl *N,N'*-di(2-chloroethyl) phosphoric acid diamide; β-D-glucosylisophosphoramide mustard; D-19575. $C_{10}H_{21}Cl_2N_2O_7P$; mol wt 383.16. C 31.35%, H 5.52%, Cl 18.51%, N 7.31%, O 29.23%, P 8.08%. Glucose coupled to isophosphoramide mustard, the active metabolite of the alkylating agent ifosfamide, *q.v.* Enters cells through upregulated glucose transport proteins. Prepn: M. Wiessler, M. Dickes, **DE 3835772**; *eidem,* **US 5622936** (1990, 1997 both to Deutsches Krebsforschungszentrum Stiftung). Pharmacology and toxicity studies: J. Pohl *et al., Cancer Chemother. Pharmacol.* **35,** 364 (1995). Mechanism of action study: H. Seker *et al., Br. J. Cancer* **82,** 629 (2000). Clinical evaluation in pancreatic cancer: E. Briasoulis *et al., Eur. J. Cancer* **39,** 2334 (2003); in non-small cell lung cancer: G. Giaccone *et al., ibid.* **40,** 667 (2004). Review of pharmacology and clinical development: I. Niculescu-Duvaz, *Curr. Opin. Invest. Drugs* **3,** 1527-1532 (2002).



LD_{50} in rats, mice (mg/kg): 1575, 1575 i.v.; 1470, 1470 orally (Pohl).

THERAP CAT: Antineoplastic.

4469. Glutamic Acid. [56-86-0] L-Glutamic acid; Glu; E; glutaminic acid; (*S*)-2-aminopentanedioic acid; α-aminoglutaric acid; 1-aminopropane-1,3-dicarboxylic acid; Glutacid; Glutaminol. $C_5H_9NO_4$; mol wt 147.13. C 40.82%, H 6.17%, N 9.52%, O 43.50%. Non-essential amino acid for human development; referred to as an excitatory amino acid (EAA) due to its role in neurotransmission. Isoln from wheat gluten: H. Ritthausen, *J. Prakt. Chem.* **99,** 454 (1866). Early chemistry and biochemistry: *Amino Acids and Proteins,* D. M. Greenberg, Ed. (Charles C. Thomas, Springfield, IL, 1951) 950 pp., *passim*; J. P. Greenstein, M. Winitz, *Chemistry of the Amino Acids* **vols 1-3** (John Wiley and Sons, Inc., New York, 1961) pp. 1929-1954, *passim*; C. W. Huffman, W. G. Skelly, *Chem. Rev.* **63,** 625-644 (1963). Interconversion from L-proline: S. Yoshifuji *et al., Tetrahedron Lett.* **21,** 2963 (1980). Determn in serum: C. D. Stalikas *et al., Eur. J. Clin. Chem.* **32,** 767 (1994); of naturally occurring levels in food: D. H. Daniels *et al., Food Addit. Contam.* **12,** 21 (1995). Identification as excitatory neurotransmitter: D. R. Curtis *et al., J. Physiol.* **150,** 656 (1960). Review of biosynthesis: A. Hamberger *et al., Adv. Biochem. Psychopharmacol.* **27,** 115-126 (1981); of metabolism and associated disorders: S. B. Prusiner, *Annu. Rev. Med.* **32,** 521-542 (1981). Review of receptor binding: P. A. Briley *et al., Mol. Cell. Biochem.* **39,** 347 (1981). Review as neurotransmitter: B. Engelsen, *Acta Neurol. Scand.* **74,** 337-355 (1986); E. Marmo, *Med. Res. Rev.* **8,** 441-458 (1988). Review of role in learning and memory: W. J. McEntee, T. H. Crook, *Psychopharmacology* **111,** 391-401 (1993); in Parkinson's disease: M. S. Starr, *Synapse* **19,** 264-293 (1995). *Books:* R. Powell, *Monosodium Glutamate and Glutamic Acid* (Noyes Dev. Corp., Park Ridge, N.J., 1968) 256 pp.; *Glutamic Acid: Advances in Biochemistry and Physiology* L. J. Filer, Jr. *et al.,* Eds. (Raven, New York, 1979).



Orthorhombic, bisphenoidal crystals from aq alc. d_4^{20} vac 1.538. Melts 160° with conversion to L-pyrrolidonecarboxylic acid. Sublimes at 200°. $[\alpha]_D^{22.4}$ +31.4° (6*N* HCl). pK_1 2.19; pK_2 4.25; pK_3 9.67. Soly in water (g/l); 8.64 (25°); 21.86 (50°); 55.32 (75°); 140.00 (100°). Insol in methanol, ethanol, ether, acetone, cold glacial acetic acid and common neutral solvents.

Hydrochloride. [138-15-8] Acidulin; Hypochylin. $C_5H_9NO_4.HCl$; mol wt 183.59. Orthorhombic bisphenoidal plates, dec 214°.

Sodium salt *see* Monosodium Glutamate.

Magnesium salt hydrobromide monohydrate. Magnesium glutamate hydrobromide; magnesium bromoglutamate; Psicosoma; Psychoverlan. $C_{10}H_{17}BrMgN_2O_8.H_2O$; mol wt 415.47.

DL-Form. [617-65-2] Orthorhombic crystals from water, 225-227° (dec). d_D^{20} 1.4601. Soly in water (g/l): 20.54 (25°); 49.34 (50°); 118.6 (75°); 284.9 (100°). Sparingly sol in alcohol, ether, petr ether.

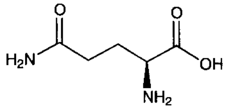
D-Form. [6893-26-1] Shiny leaflets from water. $[\alpha]_D^{20}$ −30.5° (c = 1.00 in 6*N* HCl).

THERAP CAT: Nutritional supplement. Hydrochloride as gastric acidifier. Magnesium salt hydrobromide has been used as anxiolytic.

4470. L-Glutamic Acid 5-Ethyl Ester. [1119-33-1] L-Glutamic acid γ-ethyl ester; γ-ethyl L-glutamate; Glutestere. $C_7H_{13}NO_4$; mol wt 175.18. C 47.99%, H 7.48%, N 8.00%, O 36.53%. $HOOCCH(NH_2)CH_2CH_2COOC_2H_5$. Prepn from glutamic acid, ethanol, and hydrogen chloride: Hegedus, *Helv. Chim. Acta* **31,** 737 (1948); Pravda, *Collect. Czech. Chem. Commun.* **24,** 2083 (1959); **CS 88344** (1959), *C.A.* **54,** 8660h (1960).

Hydrochloride. $C_7H_{13}NO_4.HCl$. Crystals from ethanol + ether, mp 134-136°.

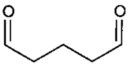
4471. Glutamine. [56-85-9] L-Glutamine; Gln; Q; 2-aminoglutaramic acid; (*S*)-2,5-diamino-5-oxopentanoic acid; glutamic acid 5-amide; Cebrogen; Glumin; Levoglutamina; Stimulina. $C_5H_{10}N_2O_3$; mol wt 146.14. C 41.09%, H 6.90%, N 19.17%, O 32.84%. Non-essential amino acid for human development; most abundant free amino acid in plasma and tissue. Isoln from sugar-beet juice: E. Schulze, E. Bosshard, *Ber.* **16,** 312 (1883). Due to ease of conversion to glutamic acid, *q.v.,* it was not isolated from protein until 1932: M. Damodoran *et al., Biochem. J.* **26,** 1704 (1932). Early chemistry and biochemistry: R. M. Archibald, *Chem. Rev.* **37,** 161-208 (1945); *Amino Acids and Proteins,* D. M. Greenberg, Ed. (Charles C. Thomas, Springfield, IL, 1951) 950 pp., *passim*; J. P. Greenstein, M. Winitz, *Chemistry of the Amino Acids* **vol 1-3** (John Wiley and Sons, Inc., New York, 1961) pp. 1929-1954, *passim.* HPLC determn in biotech samples: B. Polanuer *et al., J. Chromatogr.* **594,** 173 (1992). Review of nutritive needs: R. J. Smith, D. W. Wilmore, *J. Parenter. Enteral Nutr.* **14,** (Suppl.) 94S-99S (1990); and metabolism: W. W. Souba, *J. Nutr. Biochem.* **4,** 2-9 (1993); L. M. Castell *et al., Amino Acids* **7,** 231-243 (1994). Review of metabolism and physiologic implications: R. J. Smith, *J. Parenter. Enteral Nutr.* **14,** (Suppl.) 40S-44S (1990); B. Moskovitz *et al., Pharmacol. Res.* **30,** 61-71 (1994).



Fine opaque needles from water or dil ethanol, dec 185-186°. $[\alpha]_D^{23}$ +6.1° (c = 3.6). pK_1 2.17; pK_2 9.13. One gram dissolves in 20.8 ml water at 30°, in 38.5 ml at 18°, in 56.7 ml at 0°. Practically insol in methanol (3.5 mg/100 ml at 25°), ethanol (0.46 mg/100 ml at 23°), ether, benzene, acetone, ethyl acetate, chloroform.

DL-Form. [585-21-7] Synthesis: F. E. King, D. A. A. Kidd, *J. Chem. Soc.* **1949,** 3315; G. B. Kline, S. H. Cox, *J. Org. Chem.* **26,** 1854 (1961). Prisms from dil acetone, mp 185-186° (King); mp 173-174.5° (Kline). One gram dissolves in 38.5 ml water at 18°.

4472. Glutaraldehyde. [111-30-8] Pentanedial; glutaral; glutaric dialdehyde; 1,3-diformylpropane; Cidex; Glutarol; Novaruca; Sonacide; Ucarcide; Verucasep; Verutal. $C_5H_8O_2$; mol wt 100.12. C 59.98%, H 8.05%, O 31.96%. Prepn: C. Harries, L. Tank, *Ber.* **41,** 1701 (1908); A. C. Cope *et al., Org. Synth.* **coll. vol. IV,** 816 (1963). Toxicity data: H. F. Smyth *et al., Am. Ind. Hyg. Assoc. J.* **23,** 95 (1962). Clinical evaluation in treatment of viral warts: R. Hirose *et al., J. Dermatol.* **21,** 248 (1994). Review of role in electron microscopy: M. A. Hayat, *Micron Microsc. Acta* **17,** 115-135 (1986); of toxicology: R. O. Beauchamp, Jr. *et al., Crit. Rev. Toxicol.* **22,** 143-174 (1992); of microbiocidal activity and use as chemosterilizing agent: A. D. Russell, *Infect. Control Hosp. Epidemiol.* **15,** 724-733 (1994).



Oil, fp −14°. bp_{760} 187-189° (dec); bp_{50} 106-108°; bp_{10} 71-72°. n_D^{25} 1.43300. Vapor pressure (20°): 0.0152 torr (50% aq soln); 0.0012 torr (2% aq soln). Sol in ethanol, benzene, ether, water; volatile in steam. Polymerizes in water to a glassy form which regenerates the dialdehyde on vacuum distillation. LD_{50} of 25% soln orally in rats: 2.38 ml/kg; by skin penetration in rabbits: 2.56 ml/kg (Smyth).

Dioxime. $C_5H_{10}N_2O_2$. Crystals from water or pyridine, mp 178°. Sublimes. Treatment with hot mineral acids gives pyridine.

Caution: Potential symptoms of overexposure are irritation of eyes, skin, respiratory system; dermatitis, sensitization of skin; cough, asthma; nausea, vomiting. *See: NIOSH Pocket Guide to Chemical Hazards* (DHHS/NIOSH 97-140, 1997) p 152.

USE: Disinfectant; in sterilization of endoscopic instruments; as a tanning agent for leather; fixative for electron microscopy.

THERAP CAT: Keratolytic.

4473. Glutaric Acid. [110-94-1] Pentanedioic acid; 1,3-propanedicarboxylic acid. $C_5H_8O_4$; mol wt 132.11. C 45.46%, H 6.10%, O 48.44%. $COOH(CH_2)_3COOH$. Occurs in green sugar beets; is found in water extracts of crude wool. Manuf from cyclopentanone by oxidative ring fission with hot 50% nitric acid in the presence of vanadium pentoxide. Lab prepn by acid hydrolysis of trimethylene cyanide: Marvel, Tuley, *Org. Synth.* **5,** 69 (1925), or of methylenedimalonic ester: Otterbacher, *ibid.* **10,** 58 (1930). Several new methods: Paris *et al., Org. Synth.* **coll. vol. IV,** 496 (1963); English, Dayan, *ibid.* 499.

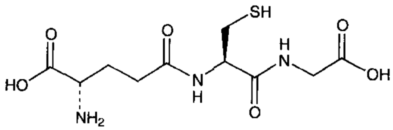
Large monoclinic prisms, mp 97.5-98°. d_4^{15} 1.429. bp_{760} 302-304° (very slight decompn); bp_{20} 200°; bp_{10} 195-198°, pK_1 (25°): 4.34; pK_2: 5.22. n_D^{106} 1.41878. Absorption spectrum: *Compt. Rend.* **189,** 915 (1929). Soly in water (g/l): at 0°: 429; at 20°: 639; at 50°: 957; at 65°: 1118. Freely sol in abs alcohol, ether; sol in benzene, chloroform; slightly in petr ether.

Dimethyl ester. $C_7H_{12}O_4$. Liquid, faint agreeable odor. d_4^{15} 1.0934. bp_{752} 213.5-214°; bp_{13} 93.5-94.5°. n_D^{20} 1.4246. Very sol in alcohol and ether.

4474. Glutaronitrile. [544-13-8] Pentanedinitrile; glutaric acid dinitrile; trimethylene dicyanide; trimethylene cyanide. $C_5H_6N_2$; mol wt 94.11. C 63.81%, H 6.43%, N 29.77%. $CN(CH_2)_3CN$. Prepd by the action of potassium cyanide on trimethylene bromide: Marvel, McColm, *Org. Synth.* **5,** 103 (1925).

Viscous liquid. Bitter-sweet taste. d^{23} 0.9888. mp −29°. bp_{760} 286°; bp_{100} 206°; bp_{60} 190°; bp_{40} 176°; bp_{20} 157°; bp_{10} 140°; bp_5 124°; $bp_{1.0}$ 91.3°. n_D^{23} 1.4365. Soluble in water, alcohol, chloroform. Insol in ether, carbon disulfide.

4475. Glutathione. [70-18-8] *N*-(*N*-L-γ-Glutamyl-L-cysteinyl)glycine; L-glutathione; glutathione-SH; GSH; Agifutol S; Copren; Deltathione; Glutamed; Glutasan; Glutathin; Glutathiol; Glutathion; Glutinal; Isethion; Neuthion; Tathiclon; Tathion; Tationil; Triptide. $C_{10}H_{17}N_3O_6S$; mol wt 307.32. C 39.08%, H 5.58%, N 13.67%, O 31.24%, S 10.43%. The major low mol wt thiol compound of the living plant or animal cell. Isoln from yeast: Hopkins, *J. Biol. Chem.* **84,** 269 (1929). Synthesis: du Vigneaud, Miller, *Biochem. Prep.* **2,** 87 (1952); Goldschmidt *et al., Ber.* **97,** 2434 (1964); Y. Ozawa *et al., Bull. Chem. Soc. Jpn.* **53,** 2592 (1980). Review of early syntheses: Jeschkeit *et al., Pharmazie* **18,** 658 (1963). Review of metabolism: A. Meister, M. E. Anderson, *Annu. Rev. Biochem.* **52,** 711-760 (1983); of metabolic role in antineoplastic chemotherapy: B. A. Arrick, C. F. Nathan, *Cancer Res.* **44,** 4224-4232 (1984). *Monographs:* S. Colowick *et al., Glutathione* (Academic Press, New York, 1954); *Glutathione,* E. M. Crook, Ed., Biochem. Soc. Symposium No. 17, London, 1958 (Cambridge University Press, 1959); *Glutathione,* L. Flohe *et al.,* Eds. (Academic Press, New York, 1974); *Glutathione: Metabolism & Function* I. M. Arias, W. B. Jackoby, Eds. (Raven, New York, 1976).



Crystals from 50% ethanol, mp 195°. $[\alpha]_D^{25}$ −18.9° (c = 4.653). $[\alpha]_D^{27}$ −21° (c = 2.74). pK_1' 2.12; pK_2' 3.53; pK_3' 8.66; pK_4' 9.12. Freely sol in water, dil alcohol, liq ammonia, dimethylformamide.

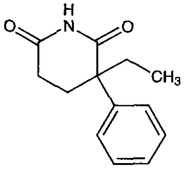
Disulfide. [27025-41-8] L-γ-Glutamyl-L-cysteinyl-glycine disulfide; *N,N'*-[dithiobis[1-[(carboxymethyl)carbamoyl]ethylene]]diglutamine; GSSG; oxidized glutathione. $C_{20}H_{32}N_6O_{12}S_2$; mol wt 612.63. Crystals, mp 123°. $[\alpha]_D^{20}$ −108° (c = 2 in water).

4476. Gluten. Protein substance of wheat which is intermixed with the starchy endosperm of the grain. Causes the carbon dioxide produced during dough fermentation to be retained by the dough in a manner which provides the porous and spongy structure of bread. Prepn from wheat: Rist, *Sugar J.* **11,** no. 9, 26 (1949), *C.A.* **43,** 9505c (1949); Christensen, **US 2583684** (1952 to Gateway Chemurgic). Amino acid composition: Pence *et al., Cereal Chem.* **27,** 335 (1950). *Reviews:* M. J. Blish "Wheat Gluten" in M. L. Anson, J. T. Edsall, *Advan. Protein Chem.* **vol. II** (Academic Press, New York, 1945) pp 337-359; Meredith, *Cereal Sci. Today* **9,** 33, 54 (1964).

Yellowish-gray powder. Practically insol in water. Partly sol in alcohol, dil acids; sol in alkalies.

USE: As adhesive and as substitute for flour.

4477. Glutethimide. [77-21-4] 3-Ethyl-3-phenyl-2,6-piperidinedione; 2-ethyl-2-phenylglutarimide; α-ethyl-α-phenylglutarimide; 3-ethyl-3-phenyl-2,6-dioxopiperidine; 3-ethyl-3-phenyl-2,6-diketopiperidine; Elrodorm; Doriden. $C_{13}H_{15}NO_2$; mol wt 217.26. C 71.87%, H 6.96%, N 6.45%, O 14.73%. Synthesis: Tagmann *et al., Helv. Chim. Acta* **35,** 1541 (1952); Salmon-Legagneur, Neveu, *Compt. Rend.* **234,** 1060 (1952); *Bull. Soc. Chim. Fr.* **1953,** 70; Hoffmann, Tagmann, **US 2673205** (1954 to Ciba). Resolution: Kukalja *et al., Croat. Chem. Acta* **33,** 41 (1961), *C.A.* **55,** 27193g (1961). Abs config of antipodes: Finch *et al., Experientia* **31,** 1002 (1975). Comprehensive description: H. Y. Aboul-Enein, *Anal. Profiles Drug Subs.* **5,** 139-187 (1976).



***dl*-Form.** Crystals from ether or from ethyl acetate + petr ether, mp 84°. uv max (methanol): 251, 257, 263 nm. Freely sol in ethyl acetate, acetone, ether, chloroform; sol in ethanol, methanol. Practically insol in water.

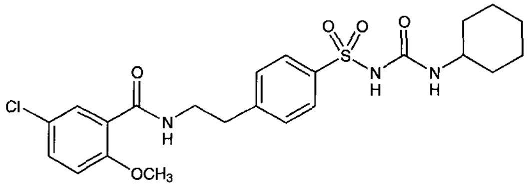
***d*-Form.** Crystals, mp 102.5-103°. $[\alpha]_D^{20}$ +176° (methanol).

***l*-Form.** Crystals, mp 102-103°. $[\alpha]_D^{20}$ −181° (methanol).

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

THERAP CAT: Sedative; hypnotic.

4478. Glyburide. [10238-21-8] 5-Chloro-*N*-[2-[4-[[[(cyclohexylamino)carbonyl]amino]sulfonyl]phenyl]ethyl]-2-methoxybenzamide; 1-[[*p*-[2-(5-chloro-*o*-anisamido)ethyl]phenyl]sulfonyl]-3-cyclohexylurea; *N*-[4-(β-(2-methoxy-5-chlorobenzamido)ethyl)-benzosulfonyl]-*N'*-cyclohexylurea; N^1-[4-[β-(2-methoxy-5-chlorobenzoylamino)ethyl]benzenesulfonyl]-N^2-cyclohexylurea; glybenzcyclamide; glibenclamide; HB-419; U-26452; Azuglucon; Bastiverit; Diabasan; Diabeta; Daonil; Duraglucon; Euglucon; Gilemal; Glimidstada; Glycolande; Libanil; Maninil; Micronase; Praeciglucon. $C_{23}H_{28}ClN_3O_5S$; mol wt 494.00. C 55.92%, H 5.71%, Cl 7.18%, N 8.51%, O 16.19%, S 6.49%. Second generation sulfonylurea with hypoglycemic activity. Prepn: Aumuller *et al., Arzneim.-Forsch.* **16,** 1640 (1966); **NL 6603398** (1966 to Boehringer, Mann.), *C.A.* **66,** 65289h (1967); **NL 6610580;** H. Weber *et al.,* **US 3454635** (1967, 1969 both to Hoechst). Pharmacology: Loubatières, Mariani, *C.R. Seances Acad. Sci. Ser. D* **265,** 643 (1967). Toxicity: Mizukami *et al., Arzneim.-Forsch.* **19,** 1413 (1969). Series of articles on synthesis, pharmacology, toxicology and clinical studies: *ibid.* 1323-1494. Effect on release of insulin, glucagon and somatostatin: S. Efendic *et al., Proc. Natl. Acad. Sci. USA* **76,** 5901 (1979). Symposium on pharmacology, mechanism of action and clinical trials: *Ann. Clin. Res.* **15,** Suppl. 37, 1-35 (1983). Comprehensive description: P. G. Takla, *Anal. Profiles Drug Subs.* **10,** 337-355 (1981). Review of pharmacology and clinical efficacy: J. M. Feldman, *Pharmacotherapy* **5,** 43-62 (1985).

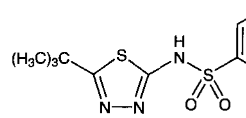


Crystals from methanol, mp 169-170° (Weber); also reported as mp 172-174° (Aumüller). pKa 5.3. Sparingly sol in water, sol in the usual organic solvents. LD_{50} in rats and mice (g/kg): >20 orally; >12.5 i.p.; >20 s.c. (Mizukami).

THERAP CAT: Antidiabetic.

4479. Glybuthiazol(e). [535-65-9] 4-Amino-*N*-[5-(1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl]benzenesulfonamide; N^1-(5-*tert*-butyl-1,3,4-thiadiazol-2-yl)sulfanilamide; sulfatertiobutylthiadiazole; 2-(*p*-aminobenzenesulfamido)-5-tertiobutyl-1,3,4-thiadiazole; glybuthizol; RP-2259; Glipasol. $C_{12}H_{16}N_4O_2S_2$; mol wt

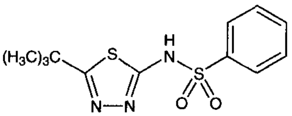
312.41. C 46.13%, H 5.16%, N 17.93%, O 10.24%, S 20.53%. Prepn: **GB 828963** (1960 to Rhône-Poulenc).



Needles from ethanol, mp 221-223°. Sol in ethanol (1.0 g/65 ml); in acetone (1.0 g/15 ml); in DMF (1.0 g/3 ml). Insol in water, ether, benzene. Forms a water-sol Na salt.

THERAP CAT: Antidiabetic.

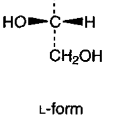
4480. Glybuzole. [1492-02-0] *N*-[5-(1,1-Dimethylethyl)-1,3,4-thiadiazol-2-yl]benzenesulfonamide; *N*-(5-*tert*-butyl-1,3,4-thiadiazol-2-yl)benzenesulfonamide; 2-benzenesulfonamido-5-*tert*-butyl-1,3,4-thiadiazole; desaglybuzole; TH-1395; RP-7891; AN-1324; Gludiase. $C_{12}H_{15}N_3O_2S_2$; mol wt 297.40. C 48.46%, H 5.08%, N 14.13%, O 10.76%, S 21.56%. Prepn: Macrae, Drain, **GB 822947** (1959 to Smith & Nephew), *C.A.* **54,** 4622h (1960); **FR M3389** (1965 to Rhône-Poulenc), *C.A.* **64,** 3553a (1966). Pharmacodynamics: Bargeton *et al., Arch. Int. Pharmacodyn.* **153,** 379 (1965).



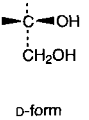
Needles, mp 163°.

THERAP CAT: Antidiabetic.

4481. Glyceraldehyde. [56-82-6] 2,3-Dihydroxypropanal; DL-glyceraldehyde; glyceric aldehyde; α,β-dihydroxypropionaldehyde. $C_3H_6O_3$; mol wt 90.08. C 40.00%, H 6.71%, O 53.28%. Obtained with its isomer dihydroxyacetone from glycerol by mild oxidation: Witzemann, *J. Am. Chem. Soc.* **36,** 2227 (1914). *See also Org. Synth.* **coll. vol. II,** 305 (1943). The equilibrium mixture of glyceraldehyde and dihydroxyacetone is called ***glycerose***. The two isomers are convertible into another through a common enediol resulting from the migration of hydrogen atoms (Lobry de Bruyn-van Eckenstein rearrangement). The equilibrium mixture plays an important role in the fermentation of sugars and in the biogenesis of constituents of the animal organism, *cf.* L.F. Fieser, M. Fieser, *Advanced Organic Chemistry* (Reinhold, New York, 1961) pp 78, 284, 405. Glyceraldehyde is the simplest aldose; the D- and L-forms are the configurational reference standard for carbohydrates. The two forms have been obtained through the action of nitrous acid on the corresponding form of 3-amino-2-hydroxypropanal: Wohl, Momber, *Ber.* **47,** 3346 (1914); Pictet, Barbier, *Helv. Chim. Acta* **4,** 924 (1921); *cf.* Baer, Fischer, *Science* **88,** 108 (1938). Prepn of L-glyceraldehyde from L-sorbose and of D-glyceraldehyde from D-fructose: Perlin, *Methods Carbohydr. Chem.* **1,** 61 (1962).



L-form



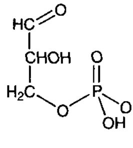
D-form

Tasteless crystals from alcohol + ether, d_{18}^{18} 1.455. mp 145°. Distills at 140-150° (bath temp) and 0.8 mm pressure. 100 ml water dissolve 3 g at 18°. Insol in benzene, petr ether, pentane. Osazone, mp 132°.

L-Form. [497-09-6] (*S*)-(−)-2,3-Dihydroxypropanol. $[\alpha]_D^{25}$ −8.7° (c = 2 in H_2O). Its dimethylacetal, $bp_{17\text{-}20}$ 126-129°. $[\alpha]_D^{26}$ −20.9° (p = 9.22).

D-Form. [453-17-8] $[\alpha]_D^{25}$ +8.7° (c = 2 in H_2O). Its dimethylacetal, bp_{17} 127-129°, bp_{10} 123-126°. $[\alpha]_D^{15}$ +21.2° (c = 18).

4482. Glyceraldehyde 3-Phosphate. [142-10-9] 2-Hydroxy-3-(phosphonooxy)propanal; 3-phosphoglyceraldehyde. $C_3H_7O_6P$; mol wt 170.06. C 21.19%, H 4.15%, O 56.45%, P 18.21%. An intermediate product of carbohydrate metabolism. Prepn of DL-form by enzymatic route: Meyerhof, Junowicz-Kocholaty, *J. Biol. Chem.* **149,** 71 (1943); by reductive cleavage of glyceraldehyde 1-benzyl ether 3-phosphoric acid: Fischer, Baer, *Ber.* **65,** 337, 1040 (1932); by hydrolysis of dimeric glyceraldehyde 1,3-diphosphoric acid: Baer, Fischer, *J. Biol. Chem.* **150,** 213 (1943); by hydrolysis of dimeric glyceraldehyde 1-bromide 3-phosphoric acid: *ibid.* 223. *See also* Baer in *Biochem. Prep.* **1,** 50 (1949). Prepn of D-form by enzymatic route: Meyerhof, Junowicz-Kocholaty, *loc. cit.;* by synthetic route: Ballou, Fischer, *J. Am. Chem. Soc.* **77,** 3329 (1955).



DL-Form calcium salt dihydrate. $C_3H_5CaO_6P.2H_2O$. Crystals, sol in water. Aq solns are not stable, particularly when alkaline. The dioxane addition compd of DL-glyceraldehyde 1-bromide 3-phosphoric acid described by Baer is relatively stable and may be stored in the refrigerator. An aq soln of the Na or K salt of glyceraldehyde-3-phosphoric acid (contg dioxane and bromide ion) is readily obtained by dissolving the dioxane compd in cold water and carefully neutralizing to pH 7.

D-Form calcium salt dihydrate. Amorphous powder. $[\alpha]_D^{25}$ +14.5° (c = 1.2 in 0.1*N* HCl calcd as the free acid). Prepn of calcium-free aq soln: Ballou, Fischer, *loc. cit.*

4483. Glyceric Acid. [473-81-4] 2,3-Dihydroxypropanoic acid; α,β-dihydroxypropionic acid. $C_3H_6O_4$; mol wt 106.08. C 33.97%, H 5.70%, O 60.33%. $CH_2OHCH(OH)COOH$. Prepn from α,β-dibromopropionic acid by treatment with silver oxide: Karrer, Klarer, *Helv. Chim. Acta* **7,** 931 (1924); from isoserine and nitrous acid: Fischer, Jacobs, *Ber.* **40,** 1069 (1907); from glycerol and nitrous acid: Mulder, *Ber.* **9,** 1902 (1876); Beilstein, *Ann.* **120,** 229 (1861). Dextrorotatory glyceric acid is obtained by the action of *Penicillia* or *Aspergilli* on the DL-form: McKenzie, Harden, *J. Chem. Soc.* **83,** 431 (1903). Levorotatory glyceric acid has been obtained by the oxidation of D(+)-glyceric aldehyde: Wohl, Schellenberg, *Ber.* **55,** 1408 (1922).

DL-Form. Syrup, dec on distn. pK (25°): 3.55. Miscible with water, alcohol, acetone. Nearly insol in ether.

L(+)-Form. Syrup. Its esters and salts are levorotatory and its salts are much more sol in water than those of the DL-form.

L-Form calcium salt. $Ca(C_3H_5O_4)_2.2H_2O$. Monoclinic sphenoidal crystals, mp 137°. One gram dissolves in 10 ml water. $[\alpha]_D^{20}$ −14.6° (c = 5).

D(−)-Form. Syrup. Its salts are dextrorotatory.

D-Form calcium salt. $Ca(C_3H_5O_4)_2.2H_2O$. Prisms, mp 138°. $[\alpha]_D^{20}$ +14.5° (c = 5).

4484. Glycerol. [56-81-5] 1,2,3-Propanetriol; glycerin; glycerine; trihydroxypropane; incorporation factor; IFP; Bulbold; Cristal; Glyceol; Ophthalgan. $C_3H_8O_3$; mol wt 92.09. C 39.13%, H 8.76%, O 52.12%. $CH_2OHCHOHCH_2OH$. Obtained from oils and fats as byproduct in the manuf of soaps and fatty acids. During World War I supplementary quantities were produced by the "Protol" fermentation process from sugar, a process based upon the fixation of acetaldehyde by sodium sulfite. Just prior to World War II the synthesis of glycerol from propylene was announced. Production from sugars by fermentation: Onishi, **US 3012945** (1961 to Noda). Identity with incorporation factor: Kuehl *et al., J. Am. Chem. Soc.* **82,** 2079 (1960). In nucleic acid the incorporation factor may exist as a bound form of glycerol. Acute toxicity: W. Bartsch *et al., Arzneim.-Forsch.* **26,** 1581 (1976). Reviews and bibliographies: J. W. Lawrie, *Glycerol and the Glycols* (New York, 1928); G. Leffingwell, M. Lesser, *Glycerin* (Brooklyn, 1945); C. S. Miner, N. N. Dalton, *Glycerol* (New York, 1953); C. Lüttgen, *Glyzerin und glyzerinähnliche Stoffe* (Heidelberg, 2nd ed., 1955); J. C. Kern in *Kirk-Othmer Encyclopedia of Chemical Technology* **vol. 11** (Wiley-Interscience, New York, 3rd ed., 1980) pp 921-932.

Syrupy liquid. Sweet warm taste. About 0.6 times as sweet as cane sugar. Hygroscopic; also absorbs H_2S, HCN, SO_2. *Contact with strong oxidizing agents such as chromium trioxide, potassium chlorate, or potassium permanganate may produce an explosion.* Neutral to litmus. Solidifies after prolonged cooling at 0° forming shiny orthorhombic crystals, mp 17.8°. bp_{760} 290.0° (dec); bp_{400} 263.0°; bp_{200} 240.0°; bp_{100} 220.1°; bp_{60} 208.0°; bp_{20} 182.2°; bp_{10} 167.2°; bp_5 153.8°; $bp_{1.0}$ 125.5°. n_D^{15} 1.4758; n_D^{20} 1.4746; n_D^{25} 1.4730. d_{15}^{15} 1.26557; d_{20}^{20} 1.26362; d_{25}^{25} 1.26201. Flash point, open cup: 350°F (176°C). Specific gravities of 95% aq soln w/w (U.S.P. grade): d_{15}^{15} 1.25270; d_{20}^{20} 1.25075; d_{25}^{25} 1.24910; 90% aq soln w/w: d_{15}^{15} 1.23950; d_{20}^{20} 1.23755; d_{25}^{25} 1.23585; 80% d_{15}^{15} 1.213; 70% d_{15}^{15} 1.185; 60% d_{15}^{15} 1.157; 50% d_{15}^{15} 1.129; 20% d_{15}^{15} 1.049; 5% d_{15}^{15} 1.0122. Viscosity (cP at 20°): 5% soln 1.143; 10% 1.311; 25% 2.095; 50% 6.050; 60% 10.96; 70% 22.94; 83% 111. Freezing points of aq solns w/w: 10% −1.6°; 30% −9.5°; 50% −23.0°; 66.7% −46.5°; 80% −20.3°; 90% −1.6°. Miscible with water, alcohol. One part dissolves in 11 parts ethyl acetate, in about 500 parts ethyl ether. Insol in benzene, chloroform, carbon tetrachloride, carbon disulfide, petr ether, oils. LD_{50} in rats (ml/kg): >20 orally; 4.4 i.v. (Bartsch).

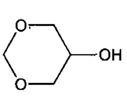
Caution: Potential symptoms of overexposure to mist are irritation of eyes, skin, respiratory system; headache, nausea, vomiting; kidney injury. *See NIOSH Pocket Guide to Chemical Hazards* (DHHS/NIOSH 97-140, 1997) p 152.

USE: As solvent, humectant, plasticizer, emollient, sweetener, in the manuf of nitroglycerol (dynamite), cosmetics, liq soaps, liqueurs, confectioneries, blacking, printing and copying inks, lubricants, elastic glues, lead oxide cements; to keep fabrics pliable; to preserve printing on cotton; for printing rollers, hectographs; to keep frost from windshields; as antifreeze in automobiles, gas meters and hydraulic jacks, in shock absorber fluids. In fermentation nutrients in the production of antibiotics. Pharmaceutic aid (humectant; solvent, vehicle). Leffingwell and Lesser (*op. cit.*) give 1583 different uses.

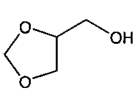
THERAP CAT: Diagnostic aid (ophthalmic).

THERAP CAT (VET): Emollient, demulcent. As a source of glucose in bovine ketosis.

4485. Glycerol Formal. Methylidinoglycerol; Glicerinformal; Sericosol N. $C_4H_8O_3$; mol wt 104.10. C 46.15%, H 7.75%, O 46.11%. Mixture of isomeric α,α′- and α,β-forms prepd from glycerin and formaldehyde: M. Schultz, B. Tollens, *Ann.* **289,** 20 (1895). Prepn and separation of isomers: H. Hibbert, N. M. Carter, *J. Am. Chem. Soc.* **50,** 3120 (1928); J. D. van Roon, *Rec. Trav. Chim.* **48,** 173 (1929). Prepn and pharmacology: P. Gimeno, **ES 475962** (1979 to Calipe), *C.A.* **93,** 26445u (1980). Toxicological evaluation for use as pharmaceutical solvent: D. M. Sanderson, *J. Pharm. Pharmacol.* **11,** 150, 446 (1959). Teratogenicity studies: V. Aliverti *et al.*, *Arch. Sci. Biol.* **61,** 89 (1977); E. Giavini, M. Prati, *Acta Anat.* **106,** 203 (1980).



α,α′-form



α,β-form

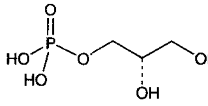
Liquid, bp_{760} 191-195°, bp_{20} 95-97°. d_4^{20} 1.215; n_D^{20} 1.451. Sol in water, alc, chloroform. pH of 10% soln: 4-6.5. LD_{50} in rats (ml/kg): 8.6 orally, 3.5 i.v. (Gimeno).

α,α′-Form. 1,3-Dioxan-5-ol; α,α′-methylene glycerin; α,α′-formaldehyde glycerol; 5-*m*-dioxanol. bp 193.8°. d_4^{25} 1.2200. n_D^{25} 1.4527.

α,β-Form. 1,3-Dioxolane-4-methanol; α,β-methylene glycerin; α,β-formaldehyde glycerol; 4-(hydroxymethyl)-1,3-dioxolane. bp 192.5°. d_4^{25} 1.2008. n_D^{25} 1.4469.

USE: Pharmaceutic aid (solvent).

4486. Glycerophosphoric Acid. [57-03-4] (DL-α-form); [17181-54-3] (β-form). Phosphoric acid glycerol esters. $C_3H_9O_6P$; mol wt 172.07. C 20.94%, H 5.27%, O 55.79%, P 18.00%. Three isomers exist: ***β-glycerophosphoric acid,*** the D(+)- and L(−)-forms of ***α-glycerophosphoric acid.*** The L-α-acid is the naturally occurring form; the β-acid, present in hydrolyzates of lecithins from natural sources, arises from migration of the phosphoryl group from the α-carbon atom. See review: Dawson, *Annu. Rep. Prog. Chem.* **55,** 365 (1958). Prepn by phosphorylation of glycerol results in a mixture of the α- and β-acids: Cherbuliez, Weniger, *Helv. Chim. Acta* **29,** 2006 (1946). Prepn and configuration of L-α-acid: Baer, Fischer, *J. Biol. Chem.* **128,** 491 (1939). Prepn of D-α-acid: *eidem, ibid.* **135,** 321 (1940). Separation of α-acid from β- and polyglycerophosphoric acids: Carrara, **IT 460219** (1950), *C.A.* **46,** 5077a (1952).



α-L-form

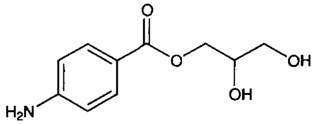
Absolute acid (commercial mixture of α- and β-acids); clear syrupy liq, mp −25°. d_4^{14} 1.59. Tends to dec during concn; hence, usually marketed as a 25-50% soln. Soluble in water, alcohol.

α-Acid L-form. [5746-57-6] (2*S*)-1-(Dihydrogen phosphate)-1,2,3-propanetriol. Syrup. Readily sol in water, methanol, ethanol. Practically insol in ether. $[\alpha]_D$ −1.45° (barium salt, c = 10.3 in 2*N* HCl).

Note: ***Phosphatidic acids*** are fatty acid diesters of glycerophosphoric acid.

USE: Absolute acid used to manuf certain glycerophosphates or to impart taste to solns of glycerophosphates which are generally used medicinally. *See also:* Calcium Glycerophosphate.

4487. Glyceryl *p*-Aminobenzoate. [136-44-7] 1,2,3-Propanetriol 1-(4-aminobenzoate); *p*-aminobenzoic acid monoglyceryl ester; monoglycerol *p*-aminobenzoate; Escalol 106. $C_{10}H_{13}NO_4$; mol wt 211.21. C 56.87%, H 6.20%, N 6.63%, O 30.30%. Prepd by controlled esterification of *p*-aminobenzoic acid with glycerol.



Semisolid, waxy mass or syrup. Faint aromatic odor. Liquefies and congeals very slowly. Soluble in methanol, ethanol, isopropanol, glycerol, propylene glycol. Insol in water, oils, fats.

USE: In cosmetic sunscreen prepns (up to 1%).

4488. Glyceryl Iodide. [554-10-9] 3-Iodo-1,2-propanediol; γ-iodopropyleneglycol; 3-iodo-1,2-dihydroxypropane. $C_3H_7IO_2$; mol wt 201.99. C 17.84%, H 3.49%, I 62.83%, O 15.84%. $ICH_2CH(OH)CH_2OH$. Prepd from 2,3-epoxy-1-propanol: Kratzl *et al.*, *Monatsh. Chem.* **93,** 49 (1962).

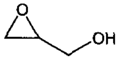
Crystals, mp 48-49°. Freely sol in water, alcohol.

4489. Glyceryl Monostearate. [31566-31-1] Octadecanoic acid monoester with 1,2,3-propanetriol; Monostearin. The commercial product is a mixture of variable proportions of glyceryl monostearate and glyceryl monopalmitate.

White, wax-like solid or wax-like beads, or flakes, mp 56-58°. Saponification value 164-170. Iodine value not more than 6. Soluble in hot organic solvents such as alcohol, benzene, ether, acetone, mineral or fixed oils. Insol in water, but may be dispersed in hot water with the aid of a small amount of soap or other suitable surface active agent.

USE: In pharmaceutical dispensing, *see* Green, *J. Am. Pharm. Assoc. Pract. Pharm. Ed.* **7,** 299 (1946).

4490. Glycidol. [556-52-5] Oxiranemethanol; 2,3-epoxy-1-propanol; 3-hydroxypropylene oxide. $C_3H_6O_2$; mol wt 74.08. C 48.64%, H 8.16%, O 43.19%. Prepd by the action of perbenzoic acid on allyl alc: Prileshajew, *Ber.* **42,** 4813 (1909); from glycerol-1-monochlorohydrin by the action of KOH in alc, or by the action of sodium in ether: Rider, Hill, *J. Am. Chem. Soc.* **52,** 1521 (1930). L-form prepd from L-1-(*p*-toluenesulfonyl)glycerol: Sowden, Fischer, *ibid.* **64,** 1291 (1942). Acute toxicity data: E. D. Thompson, R. A. Hiles, *Food Cosmet. Toxicol.* **19,** 347 (1981); E. D. Thompson, D. P. Gibson, *Food Chem. Toxicol.* **22,** 665 (1984).



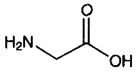
DL-Form. Slightly viscous liq. d_4^{25} 1.1143. bp_{760} 167° (decompn); $bp_{2.5}$ 66°; $bp_{0.9}$ 25°. Miscible with water. LD_{50} in female rats (g/kg): 0.42 orally, 0.20 i.p. (Thompson, Hiles). LD_{50} in male, female rats (g/kg): 0.35, 0.21 i.p.; 0.76, 0.64 orally (Thompson, Gibson).

L-Form. $[\alpha]_D^{20}$ +15° (neat).

Caution: Potential symptoms of overexposure are irritation of eyes, nose, throat and skin; narcosis. *See NIOSH Pocket Guide to Chemical Hazards* (DHHS/NIOSH 97-140, 1997) p 152. *See also Patty's Industrial Hygiene and Toxicology* **vol. 2A,** G. D. Clayton, F. E. Clayton, Eds. (John Wiley & Sons, New York, 4th ed., 1994) 422-425. This substance is reasonably anticipated to be a human carcinogen: *Report on Carcinogens, Eleventh Edition* (PB2005-104914, 2004) p III-130.

USE: Stabilizer in manuf of vinyl polymers; intermediate in synthesis of glycerol, glycidyl ethers, and amines; additive for oil and synthetic hydraulic fluids; epoxy resin diluent.

4491. Glycine. [56-40-6] Gly; G; aminoacetic acid; aminoethanoic acid; glycocoll; Gyn-Hydralin. $C_2H_5NO_2$; mol wt 75.07. C 32.00%, H 6.71%, N 18.66%, O 42.63%. Non-essential amino acid for human development. Only amino acid with no asymmetric carbon. Major inhibitory neurotransmitter. Isoln from gelatin: H. Braconnot, *Ann. Chim. Phys.* **13,** 113 (1820). Early chemistry and biochemistry: *Amino Acids and Proteins,* D. M. Greenberg, Ed. (Charles C. Thomas, Springfield, IL, 1951) 950 pp., *passim*; J. P. Greenstein, M. Winitz, *Chemistry of the Amino Acids* **vols 1-3,** (John Wiley and Sons, Inc., New York, 1961) pp. 1955-1970, *passim.* Exists in three polymorphic forms, α-, β-, and γ-: Y. Iitaka, *Nature* **183,** 390 (1959). Review of metabolism and radioprotection: S. Capalna, *Rev. Roum. Physiol.* **9,** 17-34 (1972); of metabolism in humans: A. A. Jackson, M. H. Golden, *Clin. Sci.* **58,** 517-522 (1980); in anerobes: J. R. Andreesen, *Antonie van Leeuwenhoek* **66,** 223-227 (1994). Review of role in neurotransmission: S. M. Paul in *Psychopharmacology: The Fourth Generation of Progress,* F. E. Bloom, D. J. Kupfer, Eds. (Raven Press, New York, 1995) pp 87-94. *Book: Glycine Neurotransmission,* O. P. Ottersen, J. Storm-Mathisen, Eds. (John Wiley & Sons, Chichester, U.K., 1990) pp 489.



Sweet, monoclinic prisms from alc, starts to dec at 233°, completely sintered at 290°. d 1.1607. pK_1 2.34; pK_2 9.60. pH of 0.2 molar soln in H_2O = 4.0. Adsorption on various chromatographic agents: Grettie, Williams, *J. Am. Chem. Soc.* **50,** 671 (1928). Soly in 100 ml water at 25°: 25.0 g; at 50°: 39.1 g; at 75°: 54.4 g; at 100°: 67.2 g. 100 g of abs alc dissolve about 0.06 g. Sol in 164 parts pyridine. Almost insol in ether.

Hydrochloride. $C_2H_5NO_2.HCl$. Hygroscopic prisms from HCl, mp 182°.

4492. Glycine Sulfate. [513-29-1] Triglycine sulfate. $C_6H_{17}N_3O_{10}S$; mol wt 323.28. C 22.29%, H 5.30%, N 13.00%, O 49.49%, S 9.92%. $(NH_2CH_2COOH)_3.H_2SO_4$. Prepn: Horsford, *Ann.* **60,** 1 (1846); *see also* Matthias, Miller, Remeika, *Phys. Rev.* **104,** 849 (1956). Crystal growing during prepn: Konstantinova *et al., Kristallografiya* **4,** 69-73 and 125-129 (1959).

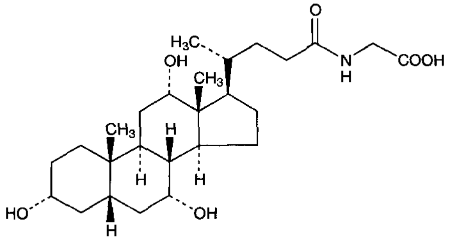
Orthorhombic crystals. Very freely sol in water. Has ferroelectric properties: Curie point 47°. Spontaneous polarization at room temp: 2.2 × 10^{-6} coul/cm^2. Coercive field 220 v/cm.

USE: In electronics research.

4493. Glycinin. [9007-93-6] Chief protein constituent of soybeans: Osborne, Campbell, *J. Am. Chem. Soc.* **20,** 419 (1898); Smith, Circle, *Ind. Eng. Chem.* **31,** 1282 (1939). *Review:* H. Neurath, K. Bailey, Eds., *The Proteins* **vol. I,** Part A (Academic Press, New York, 1953) pp 208-209, 223; *eidem, ibid.* **vol. II,** part A, (1954) pp 503, 506.

Soluble in water in the pH range 1-4, as well as above 7.

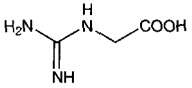
4494. Glycocholic Acid. [475-31-0] *N*-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]glycine; *N*-cholylglycine. $C_{26}H_{43}NO_6$; mol wt 465.62. C 67.07%, H 9.31%, N 3.01%, O 20.62%. The product of conjugation of cholic acid with glycine; chief ingredient of the bile of herbivorous animals. In the weakly alkaline bile fluid glycocholic acid exists as the sodium salt. Prepn from bile: Hammarsten in *Abderhalden's Handbuch der Biol. Arbeitsmethoden,* Abt. **I,** Teil 6, p 211 (1925). Prepn from cholic acid: Cortese, *J. Am. Chem. Soc.* **59,** 2532 (1937). Synthesis: Cortese, Bauman, *ibid.* **57,** 1393 (1935); Bergstrom, Norman, *Acta Chem. Scand.* **7,** 1126 (1953). Separation: Antonides, **GB 928635** (1963 to Armour). Metabolism: Norman, *Scand. J. Gastroenterol.* **5,** 231 (1970).



Sesquihydrate. Crystals from 5% alc, mp about 130°. $[\alpha]_D^{23}$ +30.8° (c = 7.5 in 95% ethanol). Anhydr form, mp 165-168°. pK 4.4. Soly in water at 15°: 0.33 g/l; in boiling water: 8.3 g/l. Is hydrolyzed to cholic acid and glycine by acids and alkalies. Forms addition compds with nitrobenzene, aniline, benzyl alcohol, benzaldehyde, triolein.

Sodium salt. $C_{26}H_{42}NNaO_6$. Crystals from 95% alcohol + ether, mp 230-240°. $[\alpha]_D^{24}$ +32° (water). Soly at 15° in water >274 g/l; in alcohol >340 g/l.

4495. Glycocyamine. [352-97-6] *N*-(Aminoiminomethyl)-glycine; *N*-amidinoglycine; guanidineacetic acid; guanidoacetic acid. $C_3H_7N_3O_2$; mol wt 117.11. C 30.77%, H 6.02%, N 35.88%, O 27.32%. Prepd from *S*-ethylthiourea hydrobromide, sodium hydroxide, and glycine: Brand, Brand, *Org. Synth.* **coll. vol. III,** 440 (1955). Crystal and molecular structure: Guha, *Acta Crystallogr.* **B29,** 2163 (1973); J. Berthou *et al., ibid.* **B32,** 1529 (1976).



Crystals, dec 280-284°. Appreciably sol in water.

THERAP CAT: In combination with betaine as cardiotonic.

4496. Glycogen. [9005-79-2] Animal starch; liver starch. $(C_6H_{10}O_5)_n$; mol wt from about 2.7 × 10^5 to 3.5 × 10^6. Reserve carbohydrate of the animal organism. High molecular wt polymer having branched-chain structure composed of D-glucopyranose residues. Distributed through the cell protoplasm. Found esp in the liver and in rested muscle. Occurs also in insects and lower plants including fungi and yeasts. Isoln by alkaline destruction of the other cell constituents: Claude Bernard, *Lecons sur le diabete* (Paris, 1877) p 553; by destruction with trichloroacetic acid: Bell, Young, *Biochem. J.* **28,** 882 (1934); by centrifugation: Meyer, Jeanloz, *Adv. Enzymol.* **3,** 112 (1943); by hydraulic pressure: Stockhausen, Silbereisen, *Biochem. Z.* **287,** 276 (1936). For biological synthesis and lysis from the Cori ester (glucose-1-phosphate) *see* the review and bibliography by Meyer, *Adv. Enzymol.* **3,** 109 (1943); *see also* Nord, *Chem. Rev.* **26,** 423 (1940); Kalckar, *ibid.* **28,** 71 (1941). Isoln from the causal agent of cotton root rot, *Phymatotrichum omnivorum* (Shear) Duggar: Ergle, *J. Am. Chem. Soc.* **69,** 2061 (1947). Studies on linkages: Bahl, Smith, *J. Org. Chem.* **31,** 2915 (1966).

White powder. $[\alpha]_D^{25}$ +196 to +197°. Sol in water with opalescence. Insol in alc. Does not reduce Fehling's soln. With iodine, brown to violet colors are produced.

4497. Glycol Dilaurate. [624-04-4] Dodecanoic acid 1,2-ethanediyl ester; ethylene dilaurate. $C_{26}H_{50}O_4$; mol wt 426.67. C 73.19%, H 11.81%, O 15.00%. $C_{11}H_{23}COOCH_2CH_2OOCC_{11}H_{23}$.

Colorless, amorphous mass, mp 50-52°. bp_{20} 188°. Insol in alcohol, ether.

USE: In lacquers and varnishes as a plasticizer.

4498. Glycolic Acid. [79-14-1] Hydroxyacetic acid; hydroxyethanoic acid. $C_2H_4O_3$; mol wt 76.05. C 31.59%, H 5.30%, O 63.11%. $HOCH_2COOH$. Constituent of sugar cane juice. Made by the action of NaOH on monochloroacetic acid; also by electrolytic reduction of oxalic acid. *Review:* Sales brochure on hydroxyacetic acid from E. I. du Pont.

Odorless, somewhat hygroscopic crystals, mp 80°. pK (25°) 3.83. Sol in water, methanol, alcohol, acetone, acetic acid, ether. pH of aq solns: 2.5 (0.5%); 2.33 (1.0%); 2.16 (2.0%); 1.91 (5.0%); 1.73 (10.0%). LD_{50} orally in rats: 1.95 g/kg, H. F. Smyth *et al., J. Ind. Hyg. Toxicol.* **23,** 259 (1941).

Caution: Mild irritant to skin, mucous membranes.

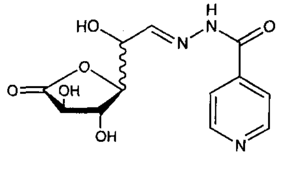
USE: In the processing of textiles, leather, and metals; in pH control, and wherever a cheap organic acid is needed, e.g. in the manuf of adhesives, in copper brightening, decontamination cleaning, dyeing, electroplating, in pickling, cleaning and chemical milling of metals.

4499. Glycol Salicylate. [87-28-5] 2-Hydroxybenzoic acid 2-hydroxyethyl ester; monoglycol salicylate; ethylene glycol monosalicylate; 2-hydroxyethyl salicylate; glysal; GL-7; Lumbinon; Phardol; Phlogont. $C_9H_{10}O_4$; mol wt 182.17. C 59.34%, H 5.53%, O 35.13%. $C_6H_4(OH)COOCH_2CH_2OH$.

Almost colorless, odorless liq. bp_{12} 169-172°. Soluble in about 110 parts water, 8 parts olive oil; very sol in alcohol, benzene, chloroform, ether.

THERAP CAT: Counterirritant, anti-inflammatory (topical).

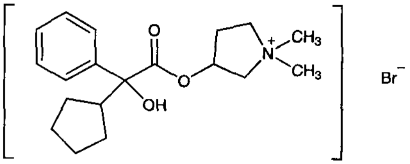
4500. Glyconiazide. [3691-74-5] D-Glucuronic acid γ-lactone 1-[(4-pyridinylcarboxyl)hydrazone]; D-glucuronolactone isonicotinoylhydrazone; isonicotinoylhydrazone of D-glucuronic acid lactone; isonicotinic acid hydrazide hydrazone with glucuronic acid lactone; Galatone; Gatalone; Glucazide; Gluconiazide; Gluronazide; Guidazide; Hydronsan; INH-G; Mycobactyl. $C_{12}H_{13}N_3O_6$; mol wt 295.25. C 48.82%, H 4.44%, N 14.23%, O 32.51%. Prepd by heating isonicotinic acid hydrazide with D-glucuronolactone in methanol: Sah, *J. Am. Chem. Soc.* **75,** 2512 (1953); Sah, **US 2940899** (1960 to U. of Calif.).



Plates and rods from methanol, needles from abs ethanol. Dec 150-160°. Freely sol in water. Practically insol in cold alc; 1.2 g dissolve in 100 ml methanol at 66°.

THERAP CAT: Antibacterial (tuberculostatic).

4501. Glycopyrrolate. [596-51-0] 3-[(Cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidinium bromide; 3-hydroxy-1,1-dimethylpyrrolidinium bromide α-cyclopentylmandelate; α-cyclopentylmandelic acid ester with 3-hydroxy-1,1-dimethylpyrrolidinium bromide; 1-methyl-3-pyrrolidyl α-cyclopentylmandelate methobromide; 1-methyl-3-pyrrolidyl α-phenyl-α-cyclopentylglycolate methobromide; 3-(2-phenyl-2-cyclopentylglycoloyloxy)-1,1-dimethylpyrrolidinium bromide; glycopyrronium bromide; AHR-504; Nodapton; Robanul; Robinul; Tarodyl; Tarodyn. $C_{19}H_{28}BrNO_3$; mol wt 398.33. C 57.29%, H 7.09%, Br 20.06%, N 3.52%, O 12.05%. Synthetic, quaternary ammonium anticholinergic. Prepn: Franko, Lunsford, *J. Med. Pharm. Chem.* **2,** 523 (1960); Lunsford, **US 2956062** (1960 to A. H. Robins). Pharmacodynamics: E. Kaltiala *et al., J. Pharm. Pharmacol.* **26,** 352 (1974). Toxicology: B. V. Franko *et al., Toxicol. Appl. Pharmacol.* **17,** 361 (1970). Clinical comparison with atropine in anaesthetic practice: F. Kongsrud, S. Sponheim, *Acta Anaesthesiol. Scand.* **26,** 620 (1982); A. I. Webb, R. M. McMurphy, *Am. J. Vet. Res.* **48,** 1733 (1987); B. V. G. Malling *et al., Br. J. Anaesth.* **60,** 426 (1988). Brief review of pharmacology and clinical use: R. K. Mirakhur, J. W. Dundee, *Anaesthesia* **38,** 1195-1204 (1983).

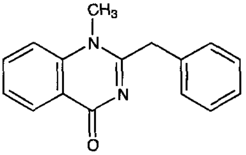


White crystals from butanone, mp 193.2-194.5°. Sol in water. LD_{50} (72 hr.) in female mice, female rats (mg/kg): 107, 196 i.p.; in male rats (mg/kg): 1150 orally (Franko).

THERAP CAT: Antispasmodic; preanesthetic medicant.

THERAP CAT (VET): Preanesthetic medicant.

4502. Glycosine. [6873-15-0] 1-Methyl-2-(phenylmethyl)-4(1*H*)-quinazolinone; 2-benzyl-1-methylquinazol-4-one; arborine. $C_{16}H_{14}N_2O$; mol wt 250.30. C 76.78%, H 5.64%, N 11.19%, O 6.39%. Found in the toothbrush plant, *Glycosmis pentaphylla* (Retz.) Corr., and *G. arborea* Corr., *Rutaceae*. Isoln from dried, powdered leaves: Chatterjee, Majumdar, *J. Am. Chem. Soc.* **76,** 2459 (1954). Identity of arborine and glycosine, structure: Chakravarti *et al., Tetrahedron* **16,** 224 (1961). Synthesis: Pakrashi *et al., Indian J. Chem.* **6,** 472 (1968); Ziegler *et al., Monatsh. Chem.* **100,** 948 (1969); T. Kametani *et al., Heterocycles* **9,** 1585 (1978).



Rhombohedral prisms from chloroform + ethyl acetate, mp 155-156°. uv max (ethanol): 231, 268, 277, 306 nm. Freely sol in chloroform, ethyl acetate, benzene, ethanol. Sparingly sol in ether.

Hydrochloride. $C_{16}H_{14}N_2O.HCl$. Leaflets from 90% ethanol, dec 209-210°.

4503. *N*-Glycylglycine. [556-50-3] $C_4H_8N_2O_3$; mol wt 132.12. C 36.36%, H 6.10%, N 21.20%, O 36.33%. $NH_2CH_2CONHCH_2COOH$. The simplest of all peptides. Prepn from 2,5-diketopiperazine: Schott *et al., J. Org. Chem.* **12,** 490 (1947); Greenstein, Winitz, *Chemistry of the Amino Acids* **vol. 2,** (New York, 1961) p 803. From tritylglycylglycine: Zervas *et al., J. Am. Chem. Soc.* **78,** 1359 (1956). From phthalylglycylglycine: Sheehan, Frank, *ibid.* **71,** 1856 (1949). From the dicyclohexylamine salt of trifluoroacetylglycylglycine: Weygand, Reiher, *Ber.* **88,** 26 (1955).

Crystals from dil alc. Crystal shape described as small tetrahedral leaves with a lustrous ball in center. Dec 262-264°. pK_1' 3.12; pK_2' 8.17. Heat of combustion: 472.4 kcal/mole. Soluble in hot water; slightly sol in ethanol. Practically insol in ether.

Hydrochloride monohydrate. $C_4H_8N_2O_3.HCl.H_2O$. Crystals from water + ethanol.

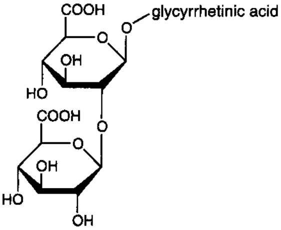
Ethyl ester hydrochloride. Crystals from abs ethanol, dec 182°.

USE: In the synthesis of more complicated peptides.

4504. Glycyrrhiza. Licorice; liquorice; sweet root. Dried rhizome and roots of *Glycyrrhiza glabra* L., var. *typica* Regel & Herder (Spanish licorice), or of *G. glabra* L., var. *glandulifera* (Waldst. & Kit.) Regel & Herder (Russian licorice), or of other varieties of *G. glabra* yielding a yellow and sweet wood, *Leguminosae*. *Habit.* Southern Europe to Central Asia. *Constit.* 6-14% glycyrrhizin (the glucoside of glycyrrhetic acid), asparagine, sugars, resin. Used chiefly in the form of glycyrrhiza syrup. *Incompat.* Acids, metallic salts.

USE: Extract and syrup as pharmaceutic aids (flavor and flavored vehicles).

4505. Glycyrrhizic Acid. [1405-86-3] (3*β*,20*β*)-20-Carboxy-11-oxo-30-norolean-12-en-3-yl 2-*O*-*β*-D-glucopyranuronosyl-*α*-D-glucopyranosiduronic acid; glycyrrhizin; glycyrrhizinic acid; glycyrrhetinic acid glycoside. $C_{42}H_{62}O_{16}$; mol wt 822.93. C 61.30%, H 7.59%, O 31.11%. Triterpene saponin used in traditional Chinese medicinal preparations for its anti-inflammatory, antiulcerous and antiallergic effects. Extraction from *Glycyrrhiza glabra* L., *Leguminosae:* Karrer, Chao, *Helv. Chim. Acta* **4,** 100 (1921); Ruzicka, Louenberger, *ibid.* **19,** 1402 (1936). From commercial glycyrrhizinum ammoniacale: Tschirch, Cederberg, *Arch. Pharm.* **245,** 97 (1907); Voss *et al., Ber.* **70,** 122 (1937). Revised method of isoln: Conn, Conn, *J. Lab. Clin. Med.* **47,** 20 (1956). Structure: Lythgoe, Trippett, *J. Chem. Soc.* **1950,** 1983. Revised structure: Marsh, Levvy, *Biochem. J.* **63,** 9 (1956). See also: I. Kitagawa *et al., Chem. Pharm. Bull.* **36,** 3710 (1988); T. Hatano *et al., ibid.* **39,** 1238 (1991). Synthesis of derivatives: Brieskorn, Sax, *Arch. Pharm.* **303,** 905 (1970). LC-MS/MS determn in plasma: Z. J. Lin *et al., J. Chromatogr. B* **814,** 201 (2005). *Review:* Nieman, *Chem. Weekbl.* **48,** 213 (1952).

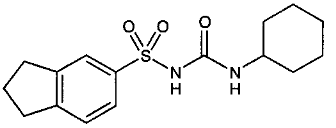


Crystals from glacial acetic acid. Intensely sweet taste. $[\alpha]_D^{17}$ +46.2° (c = 1.5 in alc). Freely sol in hot water, alcohol; practically insol in ether.

Ammonium glycyrrhizinate pentahydrate. $C_{42}H_{65}NO_{16}.5H_2O$. Needles from 75% aqueous ethanol, decomp 212-217°. $[\alpha]_D^{20}$ +46.9° (c = 1.5 in 40% ethanol). uv max: 248 nm (ε 11400). Sol in ammonia water, glacial acetic acid.

Dipotassium salt. Rizinsan K2 A2. $C_{42}H_{60}K_2O_{16}$; mol wt 899.11.

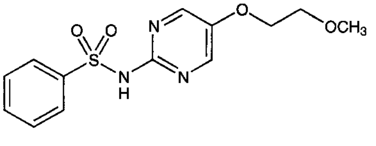
4506. Glyhexamide. [451-71-8] *N*-[(Cyclohexylamino)carbonyl]-2,3-dihydro-1*H*-indene-5-sulfonamide; 1-cyclohexyl-3-(5-indanylsulfonyl)urea; 1-cyclohexyl-3-(5-hydrindenylsulfonyl)urea; SQ-15860; Subose. $C_{16}H_{22}N_2O_3S$; mol wt 322.42. C 59.60%, H 6.88%, N 8.69%, O 14.89%, S 9.95%. Prepd from hydrindene-5-sulfonamide and cyclohexyl isocyanate: Hoehn, Breuer, **US 3097242** (1963 to Olin Mathieson). Clinical pharmacology: Grinnell *et al., Am. J. Med. Sci.* **253,** 312 (1967).



Crystals from 70% acetone, mp 153-155°.

THERAP CAT: Antidiabetic.

4507. Glymidine. [339-44-6] *N*-[5-(2-Methoxyethoxy)-2-pyrimidinyl]benzenesulfonamide; 2-benzenesulfonamido-5-(*β*-methoxyethoxy)pyrimidine; glycodiazine. $C_{13}H_{15}N_3O_4S$; mol wt 309.34. C 50.47%, H 4.89%, N 13.58%, O 20.69%, S 10.37%. Prepn: **BE 609270;** H. Priewe *et al.,* **US 3275635** (1962, 1966 both to Schering, AG); Gutsche *et al., Arzneim.-Forsch.* **14,** 373 (1964). Series of articles on pharmacology: *ibid.* 377-412. Activity: Losert *et al., ibid.* **23,** 1251 (1973). Metabolism: Soyfer *et al., Chim. Ther.* **5,** 441 (1970). Toxicity data: Kramer *et al., Arzneim.-Forsch.* **14,** 377 (1964).

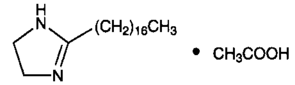


Crystals, mp 152-154°. Soly in ethanol: 0.91%; in toluene: 0.67%.

Sodium salt. [3459-20-9] SH-717; Glyconormal; Gondafon; Lycanol; Redul. $C_{13}H_{14}N_3NaO_4S$; mol wt 331.32. Crystals, mp 221-226°. Sparingly sol in alc. Soly in water at 37°: 70.5%. LD_{50} in mice, rats (g/kg): 1.48, 2.00 i.v.; 5.30, 2.85 orally (Kramer).

THERAP CAT: Antidiabetic.

4508. Glyodin. [556-22-9] 2-Heptadecyl-4,5-dihydro-1*H*-imidazole monoacetate; 2-heptadecylglyoxalidine acetate; Crag Fruit Fungicide 341. $C_{22}H_{44}N_2O_2$; mol wt 368.60. C 71.69%, H 12.03%, N 7.60%, O 8.68%. Prepn from stearic acid and ethylenediamine: Kiff, **US 2540171** (1951 to Union Carbide and Carbon).



Light orange crystals, mp 62-68°. d^{20} 1.035. Insol in water, acetone, toluene. Sol in isopropanol.

Base. Soft greasy wax, mp 94°.

USE: Agricultual fungicide.

4509. Glyoxal. [107-22-2] Ethanedial; biformyl; diformyl; oxalaldehyde. $C_2H_2O_2$; mol wt 58.04. C 41.39%, H 3.47%, O 55.13%. OHCCHO. Prepd by the oxidation of acetaldehyde by nitric or selenious acid· Lubawin, *Ber.* **8,** 768 (1875); Wyss, *Ber.* **10,** 1366 (1877); Kölln, *Ann.* **416,** 230 (1918); Riley *et al., J. Chem. Soc.* **1932,** 1881; Ronzio, Waugh, *Org. Synth.* **coll. vol. III,** 438 (1955); by hydrolysis of dichlorodioxane: Butler, Cretcher, *J. Am. Chem. Soc.* **54,** 2988 (1932). Review of commercial development: J. F. Bohmfalk *et al., Ind. Eng. Chem.* **43,** 786 (1951). Toxicity study: H. F. Smyth *et al., J. Ind. Hyg. Toxicol.* **23,** 259 (1941). *Review:* A. B. Boese *et al.* in *Glycols,* G. O. Curme, F. Johnston, Eds. (Reinhold, New York, 1952) pp 125-128.

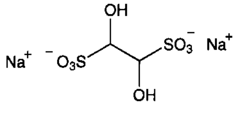
Yellow prisms or irregular pieces turning white on cooling. d^{20} 1.14. Opaque at 10°, mp 15°. bp_{776} 51°. The vapors are green and burn with a purple flame. *Explosive:* Mixtures with air may explode! $n_D^{20.5}$ 1.3826. Sol in anhydr solvents. pH of a 40% aq soln: 2.1-2.7; d_4^{20} 1.27. Polymerizes quickly on standing, on contact with water (violent reaction), or when dissolved in solvents contg water. The anhydr polymer changes to the monomer on heating. Solns of the monomer are obtained on heating the polymer with anethole, phenetole, safrole, methyl nonyl ketone, or benzaldehyde. LD_{50} in rats, guinea pigs (mg/kg): 2020, 760 orally (Smyth).

Dihydrate. $(OHCCHO)_3.2H_2O$. Crystalline powder, nonhygroscopic. More sol in hot water than in cold water. Commercially available in anhydr form as crystalline dihydrate, or as a 40% aq soln which may contain polymerization inhibitors.

Caution: Moderately irritating to skin, mucous membranes.

USE: In textiles, organic synthesis, glues, biocides.

4510. Glyoxal-Sodium Bisulfite. [517-21-5] 1,2-Dihydroxy-1,2-ethanedisulfonic acid disodium salt; glyoxal compd with sodium bisulfite. $C_2H_4Na_2O_8S_2$; mol wt 266.16. C 9.03%, H 1.51%, Na 17.28%, O 48.09%, S 24.09%. Prepn: Ronzio, Waugh, *Org. Synth.* **coll. vol. III,** 438 (1955).



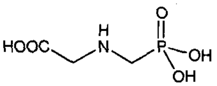
Monohydrate. Hard crystals. Faint SO_2 odor. Freely sol in water. Practically insol in alcohol.

4511. Glyoxylic Acid. [298-12-4] Oxoacetic acid; formylformic acid; glyoxalic acid; oxoethanoic acid. $C_2H_2O_3$; mol wt 74.04. C 32.44%, H 2.72%, O 64.83%. OHCCOOH. Occurs in unripe fruit and in young green leaves; has also been found in very young sugar beets. Prepd by heating dibromoacetic acid with some water: Grimaux, *Bull. Soc. Chim.* [2] **26,** 483; Cramer, *Ber.* **25,** 714 (1892); by electrolytic reduction of oxalic acid: Meyer, *Ber.* **37,** 3592 (1904); by the action of *Aspergillus niger* on calcium acetate, malonic or citric acid: Challenger *et al.*, *J. Chem. Soc.* **1927,** 205, 207. Prepn of glyoxylic acid soln for analytical use: *Beilstein* **vol. III,** 594.

Hemihydrate. Crystals from water, mp 70-75°. Also obtained in anhydr form as monoclinic crystals from water, mp 98°. Obnoxious odor. Strong, corrosive acid. $K = 4.6 \times 10^{-4}$. Deliquesces rapidly and forms a syrup on short exposure to air. Sparingly sol in alc, ether, benzene. Freely sol in water; aq solns tend to acquire a yellowish tint. Attacks most base metals except certain stainless steel alloys.

Monohydrate. Crystals, mp ~50°. Highly hygroscopic.
Caution: Irritant, corrosive.

4512. Glyphosate. [1071-83-6] *N*-(Phosphonomethyl)glycine; MON-0573. $C_3H_8NO_5P$; mol wt 169.07. C 21.31%, H 4.77%, N 8.28%, O 47.32%, P 18.32%. Broad-spectrum post-emergence, translocated herbicide. Prepn: J. E. Franz, **DE 2152826**; *idem,* **US 3799758** and **US 3853530** (1972, 1974, 1974 all to Monsanto). Metabolism and degradation in soil and water: M. L. Rueppel *et al.*, *J. Agric. Food Chem.* **25,** 517 (1977). Toxicity study: E. A. Bababunmi *et al.*, *Toxicol. Appl. Pharmacol.* **45,** 319 (1978).

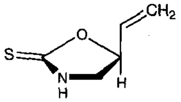


White solid, mp 230° (dec). Soly in water at 25°: 12 g/l. Insol in most organic solvents. LD_{50} in rats, mice (mg/kg): 4873, 1568 orally (Bababunmi).

Mono(isopropylamine) salt. [38641-94-0] MON-2139; Accord; Durango; Glyphomax; Glypro; Rodeo; Roundup. $C_3H_8NO_5P.C_3H_9N$; mol wt 228.18. Very sol in water.

Trimethylsulfonium salt. [81591-81-3] Sulfosate; glyphosate-trimesium; Avans-330; SC-0224; ICIA-0224; Touchdown. $C_3H_7NO_5P.C_3H_9S$; mol wt 245.23. Description of biological and physical properties: B. Trouslard, *Phytoma* **429,** 47 (1991); A. D. Baylis *et al.*, *J. Biosci.* **8,** 173 (1997). bp_{760} 110°. d 1.27. Soly in water (20°): 1050 g/l. LD_{50} in rats, mice (mg/kg): 748, 1383 orally; in rabbits (mg/kg): >2000 dermally. LC_{50} in rainbow trout (48 hrs): 4800 mg/l (Trouslard).
USE: Herbicide.

4513. Goitrin. [500-12-9] (5*S*)-5-Ethenyl-2-oxazolidinethione; 5-vinyl-2-thiooxazolidone; (−)-5-vinyl-2-oxazolidinethione. C_5H_7NOS; mol wt 129.18. C 46.49%, H 5.46%, N 10.84%, O 12.39%, S 24.82%. An antithyroid compd isolated from seeds of different species of *Brassica, Cruciferae:* Astwood *et al.*, *J. Biol. Chem.* **181,** 121 (1949); Greer, *J. Am. Chem. Soc.* **78,** 1260 (1956). Stereochemistry: Kjaer *et al.*, *Acta Chem. Scand.* **13,** 144 (1959). Activity: Langer *et al.*, *Endokrinologie* **57,** 225 (1971).



Large prisms from ether, mp 50°. $[\alpha]_D^{31}$ −70.5° (c = 2 in methanol). Behaves as a weak acid; pKa 10.5. Stable in alkali, but not in acid.

4514. Gold. [7440-57-5] Au; at. wt 196.966569; at. no. 79; valences 1, 3. Group IB (11). Occurrence in the earth's crust: 0.005 ppm. One natural isotope: 197; artificial isotopes (mass numbers): 177-179, 181, 183, 185-196, 198-203. Probably the first pure metal known to man. Occurs in nature in its native form and in minute quantities in almost all rocks and in seawater. Gold ores include ***calavarite,*** ($AuTe_2$), ***sylvanite,*** [(Ag,Au)Te_2], ***petzite,*** [(Ag,Au)$_2$Te]. Methods of mining, extracting and refining: Hull, Stent in *Modern Chemical Processes* **Vol. 5** (Reinhold, New York, 1958) pp 60-71. Lab prepn of gold powder from gold pieces: Block, *Inorg. Synth.* **4,** 15 (1953). Chemistry of gold drugs in the treatment of rheumatoid arthritis: D. H. Brown, W. E. Smith, *Chem. Soc. Rev.* **9,** 217 (1980). Use as catalyst in oxidation of organic compds by NO_2: R. E. Sievers, S. A. Nyarady, *J. Am. Chem. Soc.* **107,** 3726 (1985). Least reactive metal at interfaces with gas or liquid: B. Hammer, J. K. Norskov, *Nature* **376,** 238 (1995). *Reviews: Gmelins, Gold* (8th ed.) **62,** parts 2, 3 (1954); Johnson, Davis, "Gold" in *Comprehensive Inorganic Chemistry* **vol. 3,** J. C. Bailar Jr. *et al.*, Eds. (Pergamon Press, Oxford, 1973) pp 129-186; J. G. Cohn, E. W. Stern in *Kirk-Othmer Encyclopedia of Chemical Technology* **vol. 11** (Wiley-Interscience, New York, 3rd ed., 1980) pp 972-995.

Yellow, soft metal; face-centered cubic structure; when prepared by volatilization or precipitation methods, deep violet, purple, or ruby powder, mp 1064.76°; bp 2700°. d 19.3. Hardness (Mohs') 2.5-3.0; (Brinell's) 18.5. Extremely inactive; not attacked by acids, air or oxygen. Superficially attacked by aq halogens at room temp. Reacts with aqua regia, with mixtures contg chlorides, bromides, or iodides if they can generate nascent halogens, with many oxidizing mixtures especially those contg halogens. Also with alkali cyanides, solns of thiocyanates and double cyanides.

USE: In manuf jewelry; in gold plating other metals; as a standard of currency; most frequently alloyed with silver and copper. For use in medicine, *see* Gold, Radioactive, Colloidal.

4515. Gold Monochloride. [10294-29-8] Aurous chloride. AuCl; mol wt 232.42. Au 84.75%, Cl 15.25%. Prepd by thermal decompn of gold trichloride: Biltz, Wein, *Z. Anorg. Allg. Chem.* **148,** 192 (1925); Capella, Schwab, *C.R. Hebd. Seances Acad. Sci.* **260,** 4337 (1965).

Yellowish powder. d 7.57. Dec at about 289° into gold and Cl_2. Practically insol in water, but slowly dec by it, more rapidly on heating, with formation of gold trichloride and separation of metallic gold; sol in alkali cyanides. With solns of alkali bromides, metallic gold and potassium auribromide are formed.

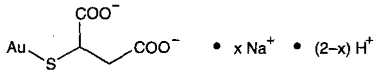
4516. Gold Monocyanide. [506-65-0] Aurous cyanide; gold cyanide. CAuN; mol wt 222.98. C 5.39%, Au 88.33%, N 6.28%. AuCN. May be prepd by decompn of $Na[Au(CN)_2]$ with HCl: Wogrinz, *Metalloberflaeche* **8,** B162 (1954).

Yellow, odorless powder; iridescent in sunlight; slowly dec in presence of moisture. When warmed with HCl, HCN is evolved. When ignited, dec into metal Au and CN. d_4^{20} 7.14. Hexagonal when cryst. Practically insol in water, alcohol, ether, dil acids; sol in ammonia, soln of NaCN; dissolved by aqua regia. On warming with concd H_2SO_4 half of the gold separates as metal.
Caution: May liberate HCN.

4517. Gold, Radioactive, Colloidal. [10043-49-9] Radioactive colloidal gold; colloidal gold ^{198}Au; radio-gold (^{198}Au) colloid; gold colloid ^{198}Au; Aurcoloid-198; Aurcoscan-198; Aureotope. Colloidal dispersion of radioactive gold (^{198}Au) for parenteral administration.

Particle diameter range, 3-7 mμ. Has half-life of 2.7 days and emits beta and gamma radiation. Stable to heat except autoclaving under pressure. Compatible with saline solns, radiopaque media and other agents; flocculated by polyvalent metal ion.
THERAP CAT: Antineoplastic.

4518. Gold Sodium Thiomalate. [12244-57-4] Mercaptobutanedioic acid monogold(1+) sodium salt; sodium aurothiomalate; Myochrysine; Shiosol; Tauredon. Disease modifying antirheumatic drug (DMARD). Mixture of the mono- ($C_4H_4AuNaO_4S$) and disodium ($C_4H_3AuNa_2O_4S$) salts of gold thiomalic acid. Prepn as the monohydrate of the disodium salt: M. Delépine, **US 1994213** (1935 to Rhone Poulenc). Detection in blood by atomic absorption spectroscopy: A. I. A. Rodgers *et al.*, *Anal. Proc.* **19,** 87 (1982). Clinical pharmacokinetics: K. L. N. Blocka *et al.*, *Clin. Pharmacokinet.* **11,** 133 (1986). Discussion of mechanisms of action: H. A. Capell, *Agents Actions Suppl.* **24,** 158 (1988). Clinical trial in rheumatoid arthritis: R. Munro *et al.*, *Ann. Rheum. Dis.* **57,** 88 (1998).



White to yellowish-white powder, metallic taste. Very sol in water. Practically insol in alcohol, ether. Aq solns are colorless to pale yellow. pH of a 5% aq soln: 5.8-6.5.
THERAP CAT: Antirheumatic.

4519. Gold Sodium Thiosulfate. [15283-45-1] Trisodium (*T*-4)-bis[monothiosulfato(2−)-*κO*,*κS*]-aurate(3−); hyposulfite of gold and sodium; sodium aurothiosulfate; Aurocidin; Aurolin; Crisalbine; Fosfocrisolo; Sanocrysin. $AuNa_3O_6S_4$; mol wt 490.19. Au 40.18%, Na 14.07%, O 19.58%, S 26.17%. $Na_3Au(S_2O_3)_2$. Prepn of dihydrate: Fordos, Gélis, *Ann. Chim. Phys.* **13,** 394 (1845); H. Brown, *J. Am. Chem. Soc.* **49,** 958 (1927); *Roger's Inorganic Pharmaceutical Chemistry,* T. O. Soine, C. O. Wilson, Eds. (Lea & Febiger, Philadelphia, 8th ed., 1967) pp 343-345. Crystal structure of dihydrate: H. Ruben *et al., Inorg. Chem.* **13,** 1836 (1974). Efficacy of antidotes: M. A. Basinger *et al., J. Rheumatol.* **12,** 274 (1985). Clinical study of contact allergy patch test reactions: K. E. McKenna *et al., Contact Dermatitis* **32,** 143 (1995). Clinical evaluation in rheumatoid arthritis: M. L. Ciompi *et al., Reumatismo* **54,** 251 (2002).

Dihydrate. [33614-49-2] White, glistening, needle-like or prismatic crystals. d 3.14. Darkens slowly on exposure to light. One gram dissolves in 2 ml water. Insol in alc and most other organic solvents. A 1:20 aq soln is neutral or slightly alkaline to litmus. LD$_{50}$ i.p. in mice: 110 mg/kg (Basinger).

Caution: Potential symptoms of overexposure via therapeutic i.m. administration are dermatitis, nausea, vomiting, diarrhea, nephritis, blood disorders, peripheral neuritis, hepatitis, encephalitis. *See Clinical Toxicology of Commercial Products,* R. E. Gosselin *et al.,* Eds. (Williams & Wilkins, Baltimore, 5th ed., 1984) p II-144.

THERAP CAT: Antirheumatic; diagnostic aid (contact allergen).

4520. Gold Stannate. [1345-24-0] Aurous stannate; C.I. Pigment Red 109; C.I. 77482; gold-tin precipitate; gold-tin purple; purple of Cassius. Contains gold, tin and oxygen; composition of commercial products varies and in some cases may be a complex mixture of gold and stannic acid. Prepn: *Colour Index* **vol. 4** (3rd ed., 1971) p 4669.

Brown powder. Practically insol in water. Sol in ammonia.

USE: Manuf ruby glass, colored enamels, and painting porcelain.

4521. Gold Trichloride. [13453-07-1] Auric chloride. $AuCl_3$; mol wt 303.33. Au 64.93%, Cl 35.06%. Conveniently prepd in the laboratory from metallic gold and iodine monochloride: Gutmann, *Z. Anorg. Allg. Chem.* **264,** 169 (1951).

Dihydrate. Dark orange-red crystals, deliquesc in moist air. d_4^{20} 3.9. Sublimes at 180° (760 mm). bp 229°. Decomp 254°. Soluble in water, alcohol, ether. *Keep well closed and protected from light.*

4522. Gold Trichloride, Acid. [16903-35-8] (*SP*-4-1)-Hydrogen tetrachloroaurate(1−); hydrochloroauric acid; aurochlorohydric acid; chloroauric acid. $AuCl_4H$; mol wt 339.79. Au 57.97%, Cl 41.74%, H 0.30%. $HAuCl_4$. Prepd according to the equation $2Au + 3Cl_2 + 2HCl \rightarrow 2HAuCl_4$: Thomsen, *Ber.* **16,** 1585 (1883); Biltz, Wein, *Z. Anorg. Allg. Chem.* **148,** 192 (1925).

Tetrahydrate. Golden-yellow to reddish-yellow, very hygroscopic and deliquesc monoclinic crystals; readily affected by sunlight. (Also available as brown crystals or cryst masses, contg 50-51% gold, and having the same properties as the yellow crystals.) Has caustic action on the skin (blisters) and then on exposure to light leaves violet-brown spots. Dec on strong heating to Cl_2, HCl, and metallic gold. d about 3.9. Very sol in water, alcohol; sol in ether. *Keep tightly closed and protected from light.*

USE: Photography, gold-plating, gilding glass and porcelain, manuf ruby glass; as a reagent for alkaloids.

4523. Gold Trihydroxide. [1303-52-2] Auric hydroxide. AuH_3O_3; mol wt 247.99. Au 79.43%, H 1.22%, O 19.35%. $Au(OH)_3$. Usually contains about $3H_2O$ and hence about 65% gold. May be prepd in lab according to the equation $2KAuCl_4 + 3Na_2CO_3 + 3H_2O \rightarrow 2Au(OH)_3 + 6NaCl + 2KCl + 3CO_2$: Lydén, *Z. Anorg. Allg. Chem.* **240,** 157 (1939).

Brown powder; dec by sunlight to metallic gold; also slowly dec with age or at 100°, and completely at 250°. Practically insol in water. Sol in soln of NaCN, in HCl or concd HNO_3. With NH_3 yields gold fulminate which *explodes easily in dry form. Protect from light.*

USE: In gold-plating solns; for decorating porcelains.

4524. Gold Trioxide. [1303-58-8] Auric oxide; gold sesquioxide; gold oxide. Au_2O_3; mol wt 441.93. Au 89.14%, O 10.86%. Prepd from the hydroxide: Roseveare, Buehner, *J. Am. Chem. Soc.* **49,** 1221 (1927).

Brown powder; begins to evolve oxygen at 110°; at 250° it is entirely dec to metallic gold; also slowly dec by sunlight. Practically insol in water. Sol in HCl, concd HNO_3 and in NaCN soln. *Keep protected from light.*

4525. Gold Trisulfide. [1303-61-3] Auric sulfide. Au_2S_3; mol wt 490.13. Au 80.37%, S 19.63%. Prepd by treating dry lithium aurichloride $Li(AuCl_4)$ with hydrogen sulfide at −10°. The reaction product consists of HCl, lithium chloride, and auric sulfide. The lithium chloride can be removed by extraction with alcohol. *Ref:* Antony, Lucchesi, *Gazz. Chim. Ital.* **19,** 552 (1889). Prepd from $AuCl_3$ or $HAuCl_4$ and H_2S in abs ether at low temp: Guthier, Dürrwachter, *Z. Anorg. Allg. Chem.* **121,** 266 (1922).

Black powder. Heating to 200° dec it into its elements.

USE: In photography.

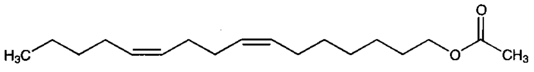
4526. Goserelin. [65807-02-5] 6-[*O*-(1,1-Dimethylethyl)-D-serine]-10-deglycinamideluteinizing hormone-releasing factor (pig) 2-(aminocarbonyl)hydrazide; D-Ser(Bu^t)^{6}Azgly^{10}-gonadorelin; D-Ser(Bu^t)^{6}Azgly^{10}-luliberin; ICI-118630. $C_{59}H_{84}N_{18}O_{14}$; mol wt 1269.41. C 55.82%, H 6.67%, N 19.86%, O 17.65%. Synthetic peptide agonist analog of LH-RH, *q.v.* Prepn: A. S. Dutta *et al.,* **DE 2720245**; *eidem,* **US 4100274** (1977, 1978 both to I.C.I.); *eidem, J. Med. Chem.* **21,** 1018 (1978). Radioimmunoassay in serum: R. N. Clayton *et al., Clin. Endocrinol.* **22,** 453 (1985). Endocrine effects in women: C. P. West, D. T. Baird, *ibid.* **26,** 213 (1987). Review of pharmacokinetics and therapeutic efficacy in sex hormone related disorders: P. Chrisp, K. L. Goa, *Drugs* **41,** 254-288 (1991). Clinical trial in treatment of uterine fibroids: J. Gerris *et al., Horm. Res.* **45,** 279 (1996); in prostate cancer: M. Bolla *et al., N. Engl. J. Med.* **337,** 295 (1997).

5-oxoPro–His–Trp–Ser–Tyr–D-Ser(*t*-Bu)–Leu–Arg–Pro–$NHNHCONH_2$

Acetate. Zoladex. $C_{59}H_{84}N_{18}O_{14}.xC_2H_4O_2$, where x = 1 to 2.4. Off-white powder. Freely sol in acetic acid; sol in water, 0.1M HCl, 0.1M NaCl, DMF, DMSO. Insol in acetone, chloroform, ether.

THERAP CAT: Antineoplastic (hormonal).

4527. Gossyplure. [50933-33-0] 7,11-Hexadecadien-1-ol acetate. $C_{18}H_{32}O_2$; mol wt 280.45. C 77.09%, H 11.50%, O 11.41%. Sex pheromone of pink bollworm, *Pectinophora gossypiella* (Saunders): Hummel *et al., Science* **181,** 873 (1973). Isoln and prepn of 1:1 mixture of (*Z,Z*) and (*Z,E*) isomers: B. A. Bierl *et al., J. Econ. Entomol.* **67,** 211 (1974). Improved prepn: R. J. Anderson, C. A. Hendrick, **US 3919329** (1975 to Zoecon); *eidem, J. Am. Chem. Soc.* **97,** 4327 (1975). Stereoselective synthesis of isomers: K. Mori *et al., Agric. Biol. Chem.* **38,** 1551 (1974); *eidem, Tetrahedron* **31,** 1846 (1975); H. Su, P. G. Mahany, *J. Econ. Entomol.* **67,** 319 (1974); H. J. Bestmann *et al., Tetrahedron Lett.* **1976,** 353; J. M. Muchowski, M. C. Venuti, *J. Org. Chem.* **46,** 459 (1981). Activity of isomers: H. M. Flint *et al., Environ. Entomol.* **6,** 274 (1977). Degradn: R. D. Henson, *ibid.* 821.



(*Z,Z*) - form

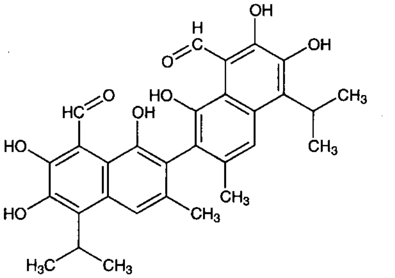
Yellow liquid. Sol in most org solvents. Extremely flammable.

***(Z,Z)*-Form.** [52207-99-5] bp 130-132°. n_D^{21} 1.4592.

***(Z,E)*-Form.** [53042-79-8] bp 132-134°. n_D^{21} 1.4591.

USE: Insect attractant.

4528. Gossypol. [303-45-7] 1,1′,6,6′,7,7′-Hexahydroxy-3,3′-dimethyl-5,5′-bis(1-methylethyl)[2,2′-binaphthalene]-8,8′-dicarboxaldehyde; 2,2′-bis[1,6,7-trihydroxy-3-methyl-5-isopropyl-8-aldehydonaphthalene]; 2,2′-bis[8-formyl-1,6,7-trihydroxy-5-isopropyl-3-methylnaphthalene]. $C_{30}H_{30}O_8$; mol wt 518.55. C 69.49%, H 5.83%, O 24.68%. Yellow pigment found in cottonseed; functions as a natural insecticide in plants. Name derived from the botanical name of the cotton plant, *Gossypium* L., *Malvaceae.* Isoln: J. Longmore, *J. Soc. Chem. Ind.* **5,** 200 (1886); L. Marchlewski, *J. Prakt. Chem.* **60,** 84 (1899); K. N. Campbell *et al., J. Am. Chem. Soc.* **59,** 1723 (1937). Structural studies: R. Adams *et al., ibid.* **60,** 2193 (1938). Synthesis: Edwards, *J. Am. Oil Chem. Soc.* **47,** 441 (1970). NMR studies: J. W. Jaroszewski *et al., NMR Spectrosc. Drug Res.* **26,** 75 (1988). Vibrational CD structural studies: T. B. Freedman *et al., Chirality* **15,** 196 (2003). Prepn of enantiomers: M. K. Dowd, *ibid.* 486. HPLC determn: G. B. Marcelle *et al., J. Pharm. Sci.* **73,** 396 (1984). Metabolism studies: M. B. Abou-Donia *et al., Lipids* **5,** 938 (1970). Mechanism of action study: C.-Y. G. Lee *et al., Mol. Cell. Biochem.* **47,** 65 (1982). Structure-activity study in tumor cell lines: M. D. Shelley *et al., Anti-Cancer Drugs* **11,** 209 (2000). Clinical evaluation in malignant glioma: P. Bushunow *et al., J. Neuro-Oncol.* **43,** 79 (1999); in male contraception: E. M. Coutinho *et al., Contraception* **61,** 61 (2000). Review of chemistry: R. Adams *et al., Chem. Rev.* **60,** 555-574 (1960); of toxicity in livestock: S. E. Morgan, *Vet. Clinics North Am.: Food Anim. Pract.* **5,** 251-262 (1989); of clinical pharmacology and use as a male contraceptive agent: D. Wu, *Drugs* **38,** 333-341 (1989); E. M. Coutinho, *Contraception* **65,** 259-263 (2002).



Exists in 3 tautomeric forms. Yellow crystals from ether, mp 184°; from chloroform, mp 199°; from ligroin, mp 214°. *Light sensitive.* Very sol in methanol, ethanol, cold dioxane, diethylene glycol, ether, ethyl acetate, acetone, carbon tetrachloride, pyridine, chloroform, DMF, lipids. Freely sol (with slow decompn) in dil aq solns of ammonia and sodium carbonate. Slightly sol in glycerol, cyclohexane. Insol in water. Absorption max: 385 nm (ε 18000).

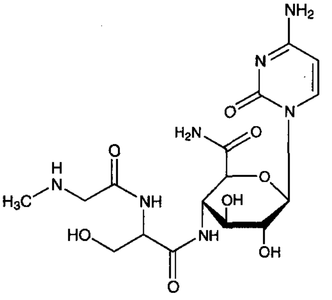
***R*-Form.** [90141-22-3] (−)-gossypol. Bright yellow crystals from acetone, mp 181-184° (dec). $[\alpha]_D^{28}$ −386 to −390° (c = 0.5 g/100 g soln in $CHCl_3$) (Dowd).

***S*-Form.** [20300-26-9] (+)-gossypol. Isoln from *Thespesia populnea*: T. J. King, L. B. de Silva, *Tetrahedron Lett.* **9,** 261 (1968); S. C. Datta *et al., Indian J. Chem.* **10,** 263 (1972). Synthesis: A. I. Meyers, J. J. Willemsen, *Tetrahedron* **54,** 10493 (1998). Bright yellow crystals from acetone, mp 181-184° (dec). $[\alpha]_D^{28}$ +386 to +390° (c = 0.5 g/100 g soln in $CHCl_3$) (Dowd). uv max (ethanol): 237.5, 277. 378 nm (log ε 4.8, 4.4, 4.2) (Datta).

Gossypol Acetic Acid. [12542-36-8] Bright yellow plates, mp 187° (Adams *et al.*).

Caution: Potentially toxic to animals overfed cottonseed products; symptoms of overexposure may include cardiac failure, shortness of breath, pulmonary edema, and reproductive effects (Morgan).

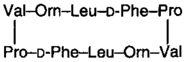
4529. Gougerotin. [2096-42-6] 1-(4-Amino-2-oxo-1(2*H*)-pyrimidinyl)-1,4-dideoxy-4-[[*N*-(*N*-methylglycyl)-D-seryl]amino]-β-D-glucopyranuronamide; 1-(4-amino-2-oxo-1(2*H*)-pyrimidinyl)-1,4-dideoxy-4-[D-2-[2-(methylamino)acetamido]hydracrylamido]-glucopyranuronamide; 1-[4-deoxy-4-(sarcosyl-D-seryl)amino-β-D-glucopyranuronamide]cytosine; aspiculamycin; asteromycin. $C_{16}H_{25}N_7O_8$; mol wt 443.41. C 43.34%, H 5.68%, N 22.11%, O 28.87%. Antibiotic substance with antibacterial and antineoplastic activity. Isoln from *Streptomyces gougerotii:* Kanzaki *et al., J. Antibiot.* **15A,** 93 (1962). Identity with asteromycin: Ikeuchi *et al., ibid.* **25,** 548 (1972). Structure: Iwasaki, *Yakugaku Zasshi* **82,** 1358 (1962). Revised structure: Fox *et al., Tetrahedron Lett.* **1968,** 6029; Watanabe *et al., Chem. Pharm. Bull.* **17,** 416 (1969). Total synthesis: *eidem, J. Am. Chem. Soc.* **94,** 3272 (1972); Lichtenthaler *et al., Tetrahedron Lett.* **1975,** 3527. Identity with aspiculamycin: Lichtenthaler *et al., ibid.* 665. Mechanism of action study: J. C. Lacal *et al., J. Antibiot.* **33,** 441 (1980). *Reviews:* Clark in *Antibiotics* **vol. 1,** D. Gottlieb, P. D. Shaw, Eds. (Springer-Verlag, New York, 1967) pp 278-282; Yukioka, *ibid.* **vol. 3,** J. W. Corcoran, F. E. Hahn, Eds. (1975) pp 448-458.



Needles, mp 211-217° (dec). $[\alpha]_D^{27}$ +53° (c = 0.8). uv max (water): 267, 235 nm (ε 9400, 9300); in 0.1*N* HCl: 275 nm (ε 13600); in 0.1*N* NaOH: 267 nm (ε 9800). LD_{50} in mice (mg/kg): 57 i.v. (Kanzaki).

4530. G-Proteins. GTP binding proteins. Distinct class of membrane associated ***guanine nucleotide binding proteins*** characterized by their function as couplers between a wide variety of receptors and their effector molecules in transmembrane signalling pathways. An example is the retinal G-protein, ***transducin***, which links the photon receptor, rhodopsin, *q.v.*, to cGMP phosphodiesterase. G-Proteins are heterotrimeric, with apparent mol wt of 100 kDa and composed of α, β, γ subunits. The α subunit contains the guanine nucleotide binding site, possesses GTPase activity, and is specific for each G-protein. β and γ subunits form a noncovalent, membrane attached complex. *Reviews:* A. M. Spiegel, *Mol. Cell. Endocrinol.* **49,** 1-16 (1987); *idem, Annu. Rep. Med. Chem.* **23,** 235-242 (1988); P. J. Casey, A. G. Gilman, *J. Biol. Chem.* **263,** 2577-2580 (1988); H. R. Bourne, *Nature* **337,** 504-505 (1989); L. Birnbaumer, *Annu. Rev. Pharmacol. Toxicol.* **30,** 675-705 (1990); M. E. Linder, A. G. Gilman, *Sci. Am.* **267,** 56-65 (July, 1992). Review of role in disease: A. C. Dolphin, *Trends Neurosci.* **10,** 53-57 (1987).

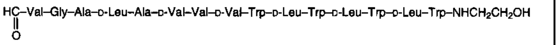
4531. Gramicidin S. [113-73-5] Gramicidin S (Soviet); gramicidin C (Soviet). $C_{60}H_{92}N_{12}O_{10}$; mol wt 1141.45. C 63.13%, H 8.12%, N 14.73%, O 14.02%. Cyclic decapeptide antibiotic produced by a strain of *Bacillus brevis.* Isoln: Gause *et al., Compt. Rend. Acad. Sci. USSR* **43,** 217 (1944), *C.A.* **39,** 1195 (1945); Gause, Brazhnikova, *Lancet* **247,** 715 (1944). More closely related to tyrocidines in biological and chemical properties than to true gramicidins, *q.q.v.* Structure: Synge, *Biochem. J.* **39,** 363 (1945); Consden *et al., ibid.* **40,** xliii (1946); **41,** 596 (1947); Battersby, Craig, *J. Am. Chem. Soc.* **73,** 1887 (1951); Erlanger, Goode, *Nature* **174,** 840 (1954). Synthesis and absorption spectrum: Schwyzer, Sieber, *Helv. Chim. Acta* **40,** 624 (1957); Waki, Izuniya, *Bull. Chem. Soc. Jpn.* **40,** 1687 (1967). Solid phase synthesis: Losse, Neubert, *Tetrahedron Lett.* **1970,** 1267; M. Ohno *et al., J. Am. Chem. Soc.* **93,** 5251 (1971). Improved synthesis via a linear pentapeptide: Y. Minematsu *et al., Tetrahedron Lett.* **1980,** 2179; via a linear decapeptide: T. Mukaiyama *et al., Chem. Lett.* **1981,** 1367. Industrial procedure: **GB 836725** (1960 to Ciba). *Review:* Y. A. Ovchinnikov, V. T. Ivanov, "The Cyclic Peptides: Structure, Conformation, and Function" in *The Proteins* **vol. V,** H. Neurath, R. L. Hill, Eds. (Academic Press, New York, 3rd ed., 1982) pp 547-555.



Hydrochloride. $C_{60}H_{92}N_{12}O_{10}.2HCl$. Prisms from ethanol + aq HCl, dec 277-278°. $[\alpha]_D^{24}$ −289° (c = 0.43 in 70% ethanol). Freely sol in alcohol; slightly sol in acetone. Practically insol in water, acids, alkalies. LD_{50} i.p. in rats: 17 mg/kg (Gause, Brazhnikova).

THERAP CAT: Topical antibacterial.

4532. Gramicidin(s). Gramicidin D (Dubos); linear gramicidins; Gramoderm. Polypeptide antibiotic complex first isolated from the mixture tyrothricin along with tyrocidine, *q.q.v.* from cultures of *Bacillus brevis:* Dubos, Hotchkiss, *J. Exp. Med.* **73,** 629 (1941); *eidem, J. Biol. Chem.* **141,** 155 (1941). Commercial extraction: Baron, **US 2534541** (1950 to Penick). Commercial preparation is a mixture of the four components, gramicidin A, B, C, and D, comprising about 87.5, 7.1, 5.1, 0.3 percent resp: Gross, Witkop, *Biochemistry* **4,** 2495 (1965). Each of the components A, B, and C consist of 2 chains, one with valine in position 1, comprising 80-95% of the component, and the other with isoleucine in position 1. Structure, characterization, and synthesis of the two isoforms of gramicidin A, *N*-formylvaline and isoleucine: Sarges, Witkop, *J. Am. Chem. Soc.* **86,** 1862 (1964); **87,** 2011, 2020 (1965); Bauer *et al., Biochemistry* **11,** 3266 (1972). Structure of gramicidin B: Sarges, Witkop, *J. Am. Chem. Soc.* **87,** 2027 (1965); of gramicidin C: *eidem, Biochemistry* **4,** 2491 (1965). Synthesis of valine-gramicidin B and C: K. Noda, E. Gross in *Chemistry and Biology of Peptides, Proc. 3rd Am. Peptide Symp.,* J. Meienhofer Ed. (Ann Arbor Science Publishers, Michigan, 1972) pp 241-250. *Review:* Hunter, Schwartz, "Gramicidins" in *Antibiotics* **I,** S. Gottlieb, P. Shaw, Eds. (Springer-Verlag, New York, 1967) pp 642-648. Comprehensive description: G. A. Brewer, *Anal. Profiles Drug Subs.* **8,** 179-218 (1979).



$$\underset{\displaystyle \overset{\|}{O}}{HC}\text{–Val–Gly–Ala–D-Leu–Ala–D-Val–Val–D-Val–Trp–D-Leu–Trp–D-Leu–Trp–D-Leu–Trp–}NHCH_2CH_2OH$$

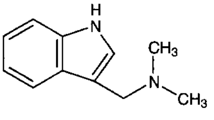
Valine-Gramicidin A

Spear-shaped or lenticular platelets, mp 229-230°. Almost insol in water (0.6 mg/100 ml). Soluble in the lower alcohols, acetic acid, pyridine. Moderately sol in dry acetone and dioxane. Practically insol in ether, hydrocarbons. Tends to form colloidal suspensions in water.

THERAP CAT: Antibacterial.

THERAP CAT (VET): Antimicrobial.

4533. Gramine. [87-52-5] *N,N*-Dimethyl-1*H*-indole-3-methanamine; 3-(dimethylaminomethyl)indole; Donaxine. $C_{11}H_{14}N_2$; mol wt 174.24. C 75.83%, H 8.10%, N 16.08%. In chlorophyll-deficient mutants of barley: Euler *et al., Z. Physiol. Chem.* **217,** 23 (1933). In the Asiatic reed *Arundo donax* L., *Gramineae:* Orechoff, Norkina, *Ber.* **68,** 436 (1935). From *Acer saccharinum* L. (the Silver Maple) and *A. rubrum* L., *Aceraceae:* Pachter *et al., J. Org. Chem.* **24,** 1285 (1959); Pachter, *J. Am. Pharm. Assoc. Sci. Ed.* **48,** 670 (1959). Synthesis: Kühn, Stein, *Ber.* **70,** 567 (1937). Biosynthesis from tryptophan in barley: Bowden, Marion, *Can. J. Chem.* **29,** 1037 (1951); O'Donovan, Leete, *J. Am. Chem. Soc.* **85,** 461 (1963); Gower, Leete, *ibid.* 3683; *see also* Gross *et al., Tetrahedron Lett.* **1971,** 4047.

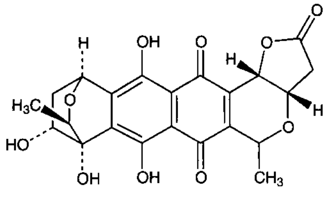


Shiny, flat needles or plates from acetone, mp 138-139°. Absorption spectrum: Kanakoa *et al., Chem. Pharm. Bull.* **8,** 294 (1960). Sol in alcohol, ether, chloroform; slightly sol in cold acetone. Practically insol in petr ether, water.

Hydrochloride. $C_{11}H_{14}N_2.HCl$. Crystals from ethanol + ether, dec 191°. Sol in water.

Methiodide. $C_{11}H_{14}N_2.CH_3I$. Crystals from methanol + benzene, mp 168-169°. Sol in water: Geissman, Armen, *J. Am. Chem. Soc.* **74,** 3916 (1952).

4534. Granaticin. [19879-06-2] (3a*S*,5*S*,8*S*,9*R*,11*R*,13b*S*,-15*R*)-3,3a,5,8,11,13b-Hexahydro-7,8,12,15-tetrahydroxy-5,9-dimethyl-8,11-ethanofuro[2,3-*e*]naphtho[2,3-*c*:6,7-*c'*]dipyran-2,6,-13(9*H*)-trione; antibiotic WR 141; litmomycin. $C_{22}H_{20}O_{10}$; mol wt 444.39. C 59.46%, H 4.54%, O 36.00%. Antibiotic substance produced by *Streptomyces olivaceus* from soil of Portuguese West Africa. Isoln and antibacterial activity: R. Corbaz *et al., Helv. Chim. Acta* **40,** 1262 (1957). Determn by microbiological diffusion assay: A. Ricicova, M. Podojil, *Folia Microbiol.* **10,** 299 (1965). Isoln of granaticin B, the α-L-rhodinoside of granaticin: S. Barcza *et al., Helv. Chim. Acta* **49,** 1736 (1966); **FR 1525993;** W. Keller, H. Zaehner, **US 3836642** (1968, 1974 both to Ciba-Geigy). Structure of granaticin and granaticin B: W. Keller-Schierlein *et al., Helv. Chim. Acta* **51,** 1257 (1968); M. Brufani, M. Dobler, *ibid.* 1269; *Naturally Occurring Quinones,* R. H. Thomson, Ed. (Academic Press, New York, 2nd ed., 1971) pp 298-302. Identity of granaticin with antibiotic litmomycin: C.-J. Chang *et al., J. Antibiot.* **28,** 156 (1975). Biosynthesis: C. E. Snipes *et al., J. Nat. Prod.* **42,** 627 (1979); *eidem, J. Am. Chem. Soc.* **101,** 701 (1979). Total synthesis of (±)-form: K. Nomura *et al., ibid.* **109,** 3402 (1987); of the natural (−)-form: K. Okazaki *et al., Chem. Commun.* **1989,** 354. Cytotoxic action on carcinoma cells: E. Sturdik, L. Drobnica, *Neoplasma* **30,** 3 (1983). Inhibition of RNA synthesis: A. Ogilvie *et al., Biochem. J.* **152,** 517 (1975); P. Heinstein, *J. Pharm. Sci.* **71,** 197 (1982).

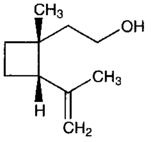


Deep red, garnet-like crystals from acetone, dec 204-206°. Also reported as mp 211-213° (dec). Acts as an indicator: red in acids, blue in alkalies. Absorption max (abs ethanol): 223, 286, 532, 576 nm (log ε 4.58, 3.76, 3.87, 3.75).

Tetraacetylgranaticin. [1401-59-8] $C_{30}H_{28}O_{14}$. Yellow crystals from alc, mp 242-243°. $[\alpha]_D^{20}$ −100° (c = 0.818 in chloroform).

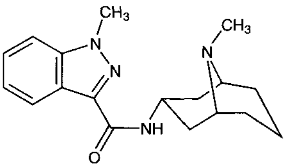
Granaticin B. [19879-03-9] $C_{28}H_{30}O_{12}$; mol wt 558.53. Red crystalline solid from methanolic-HCl, mp 117-119°. $[\alpha]_D^{22}$ +17.2° (c = 0.83 in pyridine). Absorption max (methanol): 223, 285, 527, 566 nm (log ε 4.42, 3.68, 3.76, 3.57).

4535. Grandisol. [26532-22-9] (1*R*-*cis*)-1-Methyl-2-(1-methylethenyl)cyclobutaneethanol; *cis*-(+)-2-isopropenyl-1-methylcyclobutaneethanol; (+)-(1*R*,2*S*)-1-(2'-hydroxyethyl)-1-methyl-2-isopropenylcyclobutane. $C_{10}H_{18}O$; mol wt 154.25. C 77.87%, H 11.76%, O 10.37%. Major component of ***grandlure***, the sex pheromone of the boll weevil (*Anthonomus grandis,* Boheman). Isoln and synthesis: J. H. Tumlinson *et al., Science* **166,** 1010 (1969); *eidem, J. Org. Chem.* **36,** 2616 (1971). Synthesis of optically active grandisol: P. D. Hobbs, P. D. Magnus, *Chem. Commun.* **1974,** 856; *eidem, J. Am. Chem. Soc.* **98,** 4594 (1976); K. Mori, *Tetrahedron* **34,** 915 (1978); of enantiomerically pure grandisol: J. B. Jones *et al., Can. J. Chem.* **60,** 2007 (1982). Synthesis of racemate: B. M. Trost *et al., J. Am. Chem. Soc.* **99,** 3088 (1977). Short stereoselective synthesis of (±)-grandisol: I. Aljancic-Solaja *et al., Helv. Chim. Acta* **70,** 1302 (1987). Review of syntheses: J. A. Katzenellenbogen, *Science* **194,** 139-148 (1976); J. M. Brand *et al., Fortschr. Chem. Org. Naturst.* **37,** 18-29 (1979), *see also* refs pp 157-190; K. Mori, "The Synthesis of Insect Pheromones" in *The Total Synthesis of Natural Products* **vol. 4,** J. ApSimon, Ed. (Wiley-Interscience, New York, 1981) pp 80-85.



Liquid, bp$_{1.0}$ 50-60°. $[\alpha]_D^{21.5}$ +18.5° (c = 1 in hexane). n_D^{20} 1.4748.

4536. Granisetron. [109889-09-0] 1-Methyl-*N*-[(3-*endo*)-9-methyl-9-azabicyclo[3.3.1]non-3-yl]-1*H*-indazole-3-carboxamide. $C_{18}H_{24}N_4O$; mol wt 312.41. C 69.20%, H 7.74%, N 17.93%, O 5.12%. Specific serotonin ($5HT_3$) receptor antagonist. Prepn: F. D. King, **EP 200444;** *idem,* **US 4886808** (1986, 1989 both to Beecham). $5HT_3$ receptor binding study: G. J. Kilpatrick *et al., Nature* **330,** 746 (1987). Series of articles on pharmacology and clinical trials to prevent chemotherapy-induced emesis: *Semin. Oncol.* **22,** Suppl. 10, 1-30 (1995).



Hydrochloride. [107007-99-8] BRL-43694A; Kytril. $C_{18}H_{24}N_4O.HCl$; mol wt 348.87. White to off-white solid, mp 290-292°. Readily sol in water at 20°.

THERAP CAT: Antiemetic.

4537. Granulocyte Colony-Stimulating Factor. [143011-72-7] CSF-β; G-CSF; GM-DF; MGI-2; pluripoietin. Hematopoietic growth factor that stimulates the development of committed progenitor cells to neutrophils and enhances the functional activities of the mature end-cell. Glycoprotein of mol wt 18-22 kDa; produced in response to specific stimulation by a variety of cells including monocytes, fibroblasts and endothelial cells. Murine and human molecules exhibit cross species reactivity. Originally identified as a differentiation factor for murine leukemic cells. Characterization in mouse serum: J. Lotem *et al., Int. J. Cancer* **25,** 763 (1980); A. W. Burgess, D. Metcalf, *ibid.* **26,** 647 (1980). Purification of murine G-CSF: N. A. Nicola *et al., J. Biol. Chem.* **258,** 9017 (1983); of human G-CSF: K. Welte *et al., Proc. Natl. Acad. Sci. USA* **82,** 1526 (1985); N. Nicola *et al., Nature* **314,** 625 (1985); H. Nomura *et al., EMBO J.* **5,** 871 (1986). Production of human G-CSF by recombinant DNA technology: L. M. Souza *et al., Science* **232,** 61 (1986); S. Nagata *et al., Nature* **319,** 415 (1986). Review of clinical potential and comparison with GM-CSF: W. P. Steward, *Lancet* **342,** 153-157 (1993). *Reviews:* G. D. Demetri, J. D. Griffin, *Blood* **78,** 2791-2808 (1991); L. S. Tkatch, D. J. Tweardy, *Lymphokine Cytokine Res.* **12,** 477-488 (1993). Review of role in infectious diseases: D. C. Dale *et al., J. Infect. Dis.* **172,** 1061-1075 (1995).

Filgrastim. [121181-53-1] *N*-L-Methionylcolony-stimulating factor (human clone 1034); recombinant methionyl human G-CSF; r-metHuG-CSF; KRN-8601; Neupogen. 175 amino acid peptide produced in *E. coli* by recombinant DNA technology; mol wt 18.8 kDa. Differs from endogenous human G-CSF by the addition of an *N*-terminal methionine and the absence of glycosylation. Prepn: L. M. Souza, **EP 237545** (1987 to Kirin-Amgen); *idem,* **US 5580755** (1996 to Amgen). Clinical trial in severe chronic neutropenia: D. C. Dale *et al., Blood* **81,** 2496 (1993). Book: *Filgrastim in Clinical Practice,* G. Morstyn, T. M. Dexter, Eds. (Marcel Dekker, New York, 1994) 351 pp.

Pegfilgrastim. [208265-92-3] 3-Hydroxypropyl-*N*-methionylcolony-stimulating factor (human) 1-ether with α-methyl-ω-hydroxypoly(oxy-1,2-ethanediyl); Neulasta. Pegylated form of filgrastim; modified by the addition of a 20 kDa linear molecule of polyethylene glycol. Pharmacology: G. Molineux *et al., Exp. Hematol.* **27,** 1724 (1999). Series of articles on chemistry, pharmacokinetics and clinical efficacy: *Pharmacotherapy* **23,** 1S-19S (2003). Review of prepn and development: G. Molineux, *Curr. Pharm. Des.* **10,** 1235-1244 (2004); of clinical experience in chemotherapy-induced neutropenia: A.-R. Waladkhani, *Eur. J. Cancer Care* **13,** 371-379 (2004).

Lenograstim. [135968-09-1] Granocyte; Neutrogin. Glycoprotein with 174 amino acids and 4% sugar chains produced in Chinese hamster ovary cells by recombinant DNA technology; mol wt ~20 kDa. Closely resembles endogenous human G-CSF. Prepn: M. Ono *et al.,* **WO 8604605**; *eidem,* **EP 215126** (1986, 1987 both to Chugai). Clinical trial in bone-marrow transplantation: C. Gisselbrecht *et al., Lancet* **343,** 696 (1994). Review of pharmacology and clinical experience: C. J. Dunn, K. L. Goa, *Drugs* **59,** 681-717 (2000).

Nartograstim. [134088-74-7] 1-(*N*-L-Methionyl-L-alanine)-3-L-threonine-4-L-tyrosine-5-L-arginine-17-L-serinecolony-stimulating factor (human clone 1034); marograstim; KW-2228; Neu-up. G-CSF mutein of 175 amino acids produced in *E. coli* by recombinant DNA technology; mol wt 18.9 kDa. Prepn: Y. Yokoo *et al.,* **JP 2234692** (1990 to Kyowa), *C.A.* **114,** 183900 (1991). *In vitro* activity: T. Suzuki *et al., Acta Haematol.* **87,** 181 (1992). ELISA determn in plasma: T. Kuwabara *et al., J. Pharmacobio-Dyn.* **25,** 121 (1992).

THERAP CAT: Hematopoietic; antineutropenic.

4538. Granulocyte-Macrophage Colony-Stimulating Factor. [83869-56-1] Colony-stimulating factor-2; CSF-2; CSFα; GM-CSF; NIF-T. Hematopoietic growth factor that stimulates the development of neutrophils and macrophages and promotes the proliferation and development of early erythroid, megakaryocytic and eosinophilic progenitor cells. Produced by endothelial cells, monocytes, fibroblasts and T lymphocytes. Inhibits neutrophil migration and enhances the functional activities of the mature end-cells. Purification of murine GM-CSF: A. W. Burgess *et al., J. Biol. Chem.* **252,** 1998 (1977); of human GM-CSF: N. A. Nicola *et al., Blood* **54,** 614 (1979); and identity with neutrophil migration inhibition factor (NIF-T): J. C. Gasson *et al., Science* **226,** 1339 (1984). Partial amino acid sequence of murine: L. G. Sparrow *et al., Proc. Natl. Acad. Sci. USA* **82,** 292 (1985). Cloning and expression of murine GM-CSF: N. M. Gough *et al., Nature* **309,** 763 (1984); of human: G. G. Wong *et al., Science* **228,** 810 (1985); F. Lee *et al., Proc. Natl. Acad. Sci. USA* **82,** 4360 (1985); M. A. Cantrell *et al., ibid.* 6250. Pharmacokinetics: W. P. Petros, *Pharmacotherapy* **12,** Suppl 2-2, 32S (1992). Clinical comparison with G-CSF: S. Blackwell, J. Crawford, *ibid.* 20S. *Review:* J. C. Gasson, *Blood* **77,** 1131-1145 (1991). Review of clinical and biological effects: S. G. Louie, B. Jung, *Am. J. Hosp. Pharm.* **50,** Suppl 3, S10-S18 (1993).

Molgramostim. [99283-10-0] Colony-stimulating factor 2 (human clone pHG25 protein moiety reduced); Sch-39300; Leucomax. Nonglycosylated peptide of 127 amino acids produced in *E. coli* by recombinant DNA technology. Mol wt 14.5 kDa. Pharmacokinetics in AIDS and ARC: R. G. Hewitt *et al., Antimicrob. Agents Chemother.* **37,** 512 (1993).

Regramostim. [127757-91-9] Colony-stimulating factor 2 (human clone pCSF-1 protein moiety reduced) glycoform GMC 89-107. Glycoprotein of 127 amino acids produced in Chinese hamster ovary cells by recombinant DNA technology. Mol wt 21-34 kDa.

Sargramostim. [123774-72-1] 23-L-Leucinecolony-stimulating factor 2 (human clone pHG25 protein moiety); BI 61.012; Leukine; Prokine. Variably glycosylated glycoprotein of 127 amino acids produced in yeast by recombinant DNA technology. Mol wt 15.5-19.5 kDa. Differs from endogenous human GM-CSF by the substitution of a leucine moiety at position 23 of the amino acid sequence. Clinical evaluation in myelodysplasia: W. J. Gradishar *et al., Blood* **80,** 2463 (1992); in Crohn's disease: J. R. Korzenik *et al., N. Engl. J. Med.* **352,** 2193 (2005).

THERAP CAT: Hematopoietic; antineutropenic.

4539. Graphite. [7782-42-5] Plumbago; black lead; mineral carbon. Obtained by mining, especially in Canada and Ceylon. Monograph: A. R. Ubbelohde, F. A. Lewis, *Graphite and Its Crystal Compounds* (Oxford, 1960). *Review:* Holliday *et al.* in *Comprehensive Inorganic Chemistry* **vol. 1,** J. C. Bailar, Jr. *et al.,* Eds. (Pergamon Press, Oxford, 1973) pp 1250-1294.

Crystallized carbon with traces of Fe, SiO_2, etc. Usually soft, black scales, crystals rare. d 2.09-2.23. Mohs' hardness = 1.0. Commercial varieties usually withstand temps up to 2820°. Sol in molten iron.

Caution: Potential symptoms of overexposure are coughing, dyspnea, black sputum, decreased pulmonary function and lung fibrosis. *See NIOSH Pocket Guide to Chemical Hazards* (DHHS/NIOSH 97-140, 1997) p 154.

USE: For "lead" pencils, refractory crucibles, stove polish; as pigment, lubricant, graphite cement; for matches and explosives, commutator brushes, anodes, arc-lamp carbons, electroplating; polishing compds, rust and needle-paper; coating for cathode ray tubes; moderator in nuclear piles.

4540. Graphite Fluoride. [11113-63-6] Fluorine compd with graphite. Non-wettable layered solid, CF_x, (0.5<x<1.3), obtained by direct fluorination of graphite at high temp. Two covalent forms have been produced by controlling the quality of the graphite and the reaction temp: $(CF)_n$ at (300°-600°) and $(C_2F)_n$ at (350°-400°). Composition and color are a function of the fluorination temp; the F/C ratio increases with increasing temp, and color changes from black to gray to white. Prepn: O. Ruff, O. Bretschneider, *Z. Anorg. Allg. Chem.* **217,** 1 (1934); and thermal/electrical characteristics: C.-C. Hung *et al., SAMPE Q.* **19,** 12 (1988). Evaluation as solid lubricant of $(CF_x)_n$: R. L. Fusaro, H. E. Sliney, *ASLE Trans.* **13,** 56 (1970); of $(C_2F)_n$: H. Miyake *et al., Proc. JSLE Int. Tribiol. Conf.* **2,** 395 (1985). Lubrication mechanism and wear life: R. L. Fusaro, *Wear* **53**, 303 (1979). Brief review of physical properties: Central Glass Co. in *Proc. BMRA Symp.*, Brussels 1983, A. Kozawa, M. Nagayama, Eds. (Battery Mat. Res. Assoc., 1984) 135-141; of prepn, properties and uses: T. Nakajima, N. Watanabe, *Chemtech* **1990**, 426-430. Book: N. Watanabe *et al.*, *Graphite Fluorides* (Elsevier Press, Amsterdam, 1988), 262 pp.

$(CF)_n$. Poly(carbon monofluoride); Cefbon-CF. Gray-white (commercial). d 2.58 g/cm^3; packed bulk density 0.7 g/cm^3. Insol in all solvents. Fluorine content: 61-64 wt%.

$(C_2F)_n$. Poly(dicarbon monofluoride); Cefbon-C_2F. Dark gray-black (commercial). d 2.79 g/cm^3; packed bulk density 0.8 g/cm^3. Insol in all solvents. Fluorine content: 49-53 wt%.

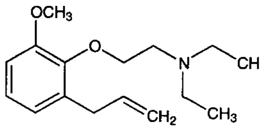
USE: Solid lubricant; as cathode material in lithium-fluoride batteries; in controlling wettability of surfaces.

4541. Graphitic Acid. [1399-57-1] Graphite oxide; graphitic oxide. This material, obtained by oxidation of graphite, was first prepd by Brodie in 1859; Hummers, Offeman, *J. Am. Chem. Soc.* **80**, 1339 (1958). Its composition is not well defined but usually given as $C_4O(OH)$: Aragon de la Cruz, Cowley, *Nature* **196**, 468 (1962), *Acta Crystallogr.* **16**, 531 (1963). Prepn and manufacture: Hummers, **US 2798878** (1957 to National Lead); Hummers, Offeman, *loc. cit.*; Ruskin, **US 2933381** and **US 2944881** (both 1960 to Union Carbide). Crystal structure: Aragon de la Cruz, Cowley, *loc. cit.*

Very light to dark brown, or yellowish-brown solid.

USE: In rocket propellant mixtures.

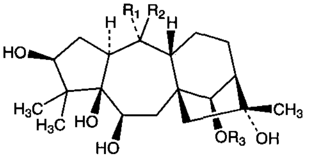
4542. Gravitol(e). [6006-09-3] 2-(2-Allyl-6-methoxyphenoxy)triethylamine; 2-methoxy-6-allylphenol diethylaminoethyl ether; Clavitol; Uterol. $C_{16}H_{25}NO_2$; mol wt 263.38. C 72.96%, H 9.57%, N 5.32%, O 12.15%. Prepn: Slotta, *Grundriss der modernen Arzneistoff-Synthese* (Stuttgart, 1931) p 118; H. Hahl, **DE 433182** (1926 to I.G. Farbenind.), *Frdl.* **15**, 1500; *Chem. Zentralbl.* **1926**, II, 2223; H. Pal'gi, *Zh. Obshch. Khim. Eng. Ed.* **28**, 2275 (1958). Pharmacology: E. Käer, G. Barkan, *Arch. Exp. Pathol. Pharmakol.* **170**, 111 (1933).



Oily liq. bp$_{10}$ 160-161°; bp$_{2\text{-}3}$ 141-144°. $n_D^{24.5}$ 1.5075. Slightly sol in water.

Hydrochloride. $C_{16}H_{26}ClNO_2$. Crystals, freely sol in water.

4543. Grayanotoxins. Toxic diterpenoids present in leaves of the various species of *Rhododendron*, *Kalmia*, and *Leucothoe*, *Ericaceae*; also found in honey from rhododendron flowers. Eighteen grayanotoxins have been isolated, the first three being the most important. Isoln of grayanotoxins I, II, III: Kakisawa *et al.*, *Tetrahedron* **21**, 3091 (1965); of IV and V: Okuno *et al.*, *ibid.* **26**, 4765 (1970); of V, VI, and VII: Hikino *et al.*, *Chem. Pharm. Bull.* **18**, 2357 (1970); of VIII, IX, X, and XI: Hikino *et al.*, *ibid.* **19**, 1289 (1971); of XII and XIII: Hikino *et al.*, *ibid.* **20**, 422 (1972). Approaches to synthesis of the grayanotoxin skeleton: T. Shiozaki *et al.*, *Tetrahedron Lett.* **1972**, 657; T. Kametani *et al.*, *Chem. Pharm. Bull.* **27**, 152 (1979); *eidem*, *Tetrahedron Lett.* **22**, 2379 (1981); *eidem*, *Tetrahedron* **37**, 3813 (1981). Toxicity study: H. Hikino *et al.*, *Toxicol. Appl. Pharmacol.* **35**, 303 (1976).



	R_1	R_2	R_3
Grayanotoxin I	OH	CH_3	$COCH_3$
Grayanotoxin III	OH	CH_3	H
Grayanotoxin II	R_1R_2 = $=CH_2$		R_3 = H

Grayanotoxin I. [4720-09-6] (3β,6β,14*R*)-Grayanotoxane-3,5,6,10,14,16-hexol 14-acetate; G-I; acetylandromedol; andromedotoxin; rhodotoxin; asebotoxin. $C_{22}H_{36}O_7$; mol wt 412.52. From *Leucothoe grayana* Max., *Ericaceae:* Miyajimi, Takei, *J. Agric. Chem. Soc. Jpn.* **10**, 1093 (1934); from *Rhododendron maximum* L., *Ericaceae:* Wood *et al.*, *J. Am. Chem. Soc.* **76**, 5689 (1954). Identity with acetylandromedol, andromedotoxin, rhodotoxin: Tallent *et al.*, *ibid.* **79**, 4548 (1957). Stereochemistry: Iwasa, Nakamura, *Tetrahedron Lett.* **1969**, 3973; Narayanan *et al.*, *ibid.* **1970**, 3943; Hikino *et al.*, *Chem. Pharm. Bull.* **18**, 1071 (1970). Approach to synthesis: Okuno, Matsumoto, *Tetrahedron Lett.* **1969**, 4077. Has hypotensive action: Moran *et al.*, *J. Pharmacol. Exp. Ther.* **110**, 415 (1954). Crystals from ethyl acetate, mp 258-260 to 267-270°, depending on rate of heating. $[\alpha]_D^{25}$ −8.8° (c = 2.3 in ethanol). Sol in hot water, alcohol, acetic acid, hot chloroform; very slightly sol in benzene, ether, petr ether. LD$_{50}$ i.p. in mice: 1.31 mg/kg (Hikino, 1976).

Grayanotoxin II. [4678-44-8] (3β,6β,14*R*)-Grayanotox-10(20)-ene-3,5,6,14,16-pentol; G-II; deacetylanhydroandromedotoxin. $C_{20}H_{32}O_5$; mol wt 352.47. From *L. grayana* Max., *Ericaceae:* Miyajimi, Takei, *loc. cit.* Identity with deacetylanhydromedotoxin: Meguri, *Yakugaku Zasshi* **79**, 1060 (1959); *C.A.* **54**, 5599g (1960). Stereochemistry: Iwasa, Nakamura, *loc. cit.*; Kumazawa, Iriye, *Tetrahedron Lett.* **1970**, 927; Yasue *et al.*, *Chem. Pharm. Bull.* **18**, 2586 (1970). Synthesis: S. Gasa *et al.*, *Tetrahedron Lett.* **1976**, 553. Columnar crystals, mp 199-200°. $[\alpha]_D^{28}$ −41.88°. LD$_{50}$ i.p. in mice: 26.1 mg/kg (Hikino, 1976).

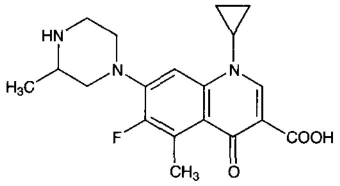
Grayanotoxin III. [4678-45-9] (3β,6β,14*R*)-Grayanotoxane-3,5,6,10,14,16-hexol; G-III; deacetylandromedotoxin. $C_{20}H_{34}O_6$; mol wt 370.48. From *L. grayana* Max., *Ericaceae:* Miyajimi, Takei, *J. Agric. Chem. Soc. Jpn.* **12**, 947 (1936), *C.A.* **30**, 6747^9 (1936). Stereochemistry: Hikino *et al.*, *Chem. Pharm. Bull.* **18**, 1071 (1970). LD$_{50}$ i.p. in mice: 0.84 mg/kg (Hikino, 1976).

4544. Green Fluorescent Protein. GFP. Class of autofluorescent proteins found in bioluminescent coelenterates where they function as energy transfer acceptors, emitting a green fluorescent light (λ_{max} = 509 nm). Acidic globular proteins consisting of 238 amino acids, monomeric mol wt ~30,000. Developed commercially as a biochemical tool to visualize cellular structure and monitor dynamic cellular events via fluorescence resonance energy transfer (FRET) assays. Purifn, characterization and energry transfer studies from *Aequorea victoria:* H. Morise *et al.*, *Biochemistry* **13**, 2656 (1974); from *Renilla reniformis:* W. W. Ward, M. J. Cormier, *J. Biol. Chem.* **254**, 781 (1979). Properties of naturally occurring proteins: M. Chalfie, *Photochem. Photobiol.* **62**, 651 (1995). Structural studies of chromophore fragment: G. N. Phillips, Jr., *Curr. Opin. Struct. Biol.* **7**, 821 (1997); B. R. Branchini *et al.*, *J. Am. Chem. Soc.* **120**, 1 (1998). Fluorescence and spectral properties of variants genetically engineered for enhanced fluorescence: G. H. Patterson *et al.*, *Biophys. J.* **73**, 2782 (1997); R. H. Stauber *et al.*, *BioTechniques* **24**, 462 (1998); for Ca^{2+} visualization: T. Nagai *et al.*, *Proc. Natl. Acad. Sci. USA* **98**, 3197 (2001). Review of expression and detection: S. R. Kain, P. Kitts, *Methods Mol. Biol.* **63**, 305-324 (1997). Review of research applications: T. Misteli, D. L. Spector, *Nat. Biotechnol.* **15**, 961-964 (1997); as reporter gene: S. R. Kain *et al.*, *BioTechniques* **19**, 650-655 (1995); as fluorescent protein tag: H.-H. Gerdes, C. Kaether, *FEBS Lett.* **389**, 44-47 (1996). Bibliography: L. J. Kricka, P. E. Stanley, *J. Biolumin. Chemilumin.* **12**, 113-134 (1997).

USE: Research tool in cell biology.

4545. Grepafloxacin. [119914-60-2] 1-Cyclopropyl-6-fluoro-1,4-dihydro-5-methyl-7-(3-methyl-1-piperazinyl)-4-oxo-3-quinolinecarboxylic acid. $C_{19}H_{22}FN_3O_3$; mol wt 359.39. C 63.50%, H 6.17%, F 5.29%, N 11.69%, O 13.36%. Fluorinated quinolone antibacterial. Prepn: J. M. Domagala *et al.*, **WO 8906649**; *eidem*, **US 4920120** (1989, 1990 both to Warner-Lambert); S. E. Hagen *et al.*, *J. Med. Chem.* **34**, 1155 (1991). Comparative *in vitro* activity: F. Marco *et al.*, *J. Antimicrob. Chemother.* **33**, 647 (1994); R. C. Arduino *et al.*, *ibid.* **34**, 403. HPLC determn in human bronchoalveolar lavage samples: J. M. Woodcock *et al.*, *FEMS Microbiol. Lett.* **119**, 315 (1994). Clinical pharmacokinetics: J. Child *et al.*, *Antimicrob. Agents Chemother.* **39**, 513 (1995). Tissue concentration in lung: P. J. Cook *et al.*, *J. Antimicrob.*

Chemother. **35,** 317 (1995). Review of pharmacology and clinical trials: A. J. Wagstaff, J. A. Balfour, *Drugs* **53,** 817-824 (1997).



Dihydrate. mp 190-192°.

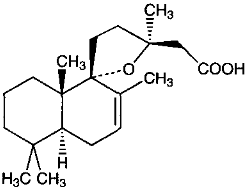
Hydrochloride. [161967-81-3] OPC-17116; Raxar. $C_{19}H_{22}FN_3O_3.HCl$; mol wt 395.86.

THERAP CAT: Antibacterial.

4546. Grindelia. Gum-plant (of California). Dried leaves and flowering tops of *Grindelia camporum* Greene or of *G. humilis* H. & A. *(G. cuneifolia* Auth.*), Compositae. Habit.* North America (California). *Constit.* Volatile oil, over 20% resin, grindelol, saponin, tannin, robustic acid.

THERAP CAT: Expectorant.

4547. Grindelic Acid. [1438-57-9] (1′*R*,4′a*S*,5*S*,8′a*S*)-4,-4′a,5,5′,6′,7′,8′,8′a-Octahydro-2′,5,5′,5′,8′a-pentamethylspiro[furan-2(3*H*),1′(4′*H*)-naphthalene]-5-acetic acid; 9,13-epoxylabd-7-en-15-oic acid. $C_{20}H_{32}O_3$; mol wt 320.47. C 74.96%, H 10.06%, O 14.98%. Major grindelane diterpenoid isolated from the resin of *Grindelia robusta* Nutt., *Compositae.* Isoln and structure: L. Panizzi *et al., Gazz. Chim. Ital.* **92,** 522 (1962). Stereochemical studies: L. Mangoni, M. Belardini, *ibid.* **92,** 1379 (1962); **93,** 455, 465 (1963). Synthesis: M. Adinolfi *et al., ibid.* **106,** 625 (1976). Absolute configuration: M. Adinolfi *et al., Phytochemistry* **27,** 1878 (1988); L. A. Paquette, H.-L. Wang, *J. Org. Chem.* **61,** 5352 (1996).



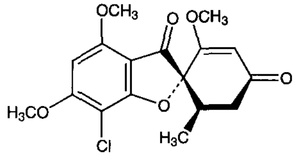
Crystals from acetic acid, mp 100-101°. $[\alpha]_D$ −102.2°.

Methyl ester. $C_{21}H_{34}O_3$. Crystals from methanol, mp 70-70.5°. $[\alpha]_D$ −134.1° (c = 1.46 in methanol).

4548. Grisein. [1391-82-8] Antibiotic substance produced by strains of *Streptomyces griseus.* Isoln: Reynolds *et al., Proc. Soc. Exp. Biol. Med.* **64,** 50 (1947); Reynolds, Waksman, *J. Bacteriol.* **55,** 739 (1948). Improved method of isoln: F. A. Kuehl, L. Chaiet, **US 2505053** (1950 to Merck & Co.); F. A. Kuehl *et al., J. Am. Chem. Soc.* **73,** 1770 (1951). Analysis of composition: $C_{40}H_{61}FeN_{10}O_{20}S$. Degradation of grisein by acid hydrolysis yielded 3-methyluracil and at least two amino acids. One of the acids appears to be glutamic acid: F. A. Kuehl *et al., loc. cit.* Probably is a mixture of components; similar or identical to albomycin, *q.v.*: Stapley, Ormond, *Science* **125,** 587 (1957); Turková *et al., Collect. Czech. Chem. Commun.* **31,** 2444 (1966). Toxicity study: V. I. Aksenov, *Veterinariya (Moscow)* **12,** 93 (1974), *C.A.* **83,** 54127d (1975). Biosynthesis: V. V. Kuklin *et al., Antibiotiki* **25,** 403 (1980), *C.A.* **93,** 146173a (1980).

Amorphous red powder. Sol in water; slightly sol in 95% alcohol. Practically insol in abs alcohol, ether, acetone, chloroform, benzene. The activity remains unchanged when an aq soln is heated to 100° for 10 min. LD_{50} in mice (mg/kg): 600 orally; 34 s.c. (Aksenov).

4549. Griseofulvin. [126-07-8] (1′*S*,6′*R*)-7-Chloro-2′,4,6-trimethoxy-6′-methylspiro[benzofuran-2(3*H*),1′-[2]cyclohexene]-3,4′-dione; 7-chloro-4,6-dimethoxycoumaran-3-one-2-spiro-1′-(2′-methoxy-6′-methylcyclohex-2′-en-4′-one); amudane; Curling factor; Fulcin; Fulvicin; Grifulvin; Grisactin; Griséfuline; Grisovin; Gris-PEG; Grysio; Lamoryl; Likuden; Polygris; Poncyl-FP; Spirofulvin; Sporostatin. $C_{17}H_{17}ClO_6$; mol wt 352.77. C 57.88%, H 4.86%, Cl 10.05%, O 27.21%. Antibiotic substance produced by *Penicillium griseofulvum* Dierckx and by *P. janczewskii* Zal. [same as *P. nigricans* (Banier)Thom]. Isoln: Oxford *et al., Biochem. J.* **33,** 240 (1939); Brian *et al., Trans. Br. Mycol. Soc.* **29,** 173 (1946); Hockenhull, Dorey *et al.,* **US 3069328, US 3069329** (both 1962 to Glaxo). Structure: Grove *et al., Chem. Ind. (London)* **1951,** 219; *J. Chem. Soc.* **1952,** 3977. Stereochemistry: MacMillan, *ibid.* **1959,** 1823; Brown, Sim, *ibid.* **1963,** 1050. Total synthesis: Brossi *et al., Helv. Chim. Acta* **43,** 1444, 2071 (1960); Taub *et al., Tetrahedron* **19,** 1 (1963); Stork, Tomasz, *J. Am. Chem. Soc.* **86,** 471 (1964); S. Danishefsky, F. J. Walker, *ibid.* **101,** 7018 (1979). Conformation: Levine, Hicks, *Tetrahedron Lett.* **1971,** 311. Crystal structure: G. Malmros *et al., Cryst. Struct. Commun.* **6,** 463 (1977). Review and evaluation of studies of carcinogenic action in laboratory animals: *IARC Monographs* **10,** 153-161 (1976). *Review:* Grove, *Q. Rev. Chem. Soc.* **17,** 1 (1963); Huber in *Antibiotics* **vol. 3,** J. W. Corcoran, F. E. Hahn, Eds. (Springer-Verlag, New York, 1975) pp 606-613. Comprehensive description: E. R. Townley, *Anal. Profiles Drug Subs.* **8,** 219-249 (1979).

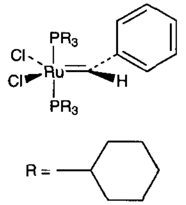


Stout octahedra or rhombs from benzene, mp 220°. $[\alpha]_D^{17}$ +370° (satd $CHCl_3$ soln). uv max: 286, 325 nm. Soly in DMF at 25°: 12 to 14 g/100 ml. Slightly sol in ethanol, methanol, acetone, benzene, $CHCl_3$, ethyl acetate, acetic acid. Practically insol in water, petr ether.

THERAP CAT: Antifungal.

THERAP CAT (VET): Antifungal.

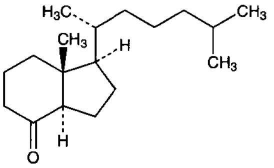
4550. Grubbs' Catalyst. [172222-30-9] (*SP*-5-31)-Dichloro(phenylmethylene)bis(tricyclohexylphosphine)ruthenium; benzylidenebis(tricyclohexylphosphine)ruthenium dichloride. $C_{43}H_{72}Cl_2P_2Ru$; mol wt 822.96. C 62.76%, H 8.82%, Cl 8.62%, P 7.53%, Ru 12.28%. Transition metal catalyst. Prepn: P. Schwab *et al., Angew. Chem. Int. Ed.* **34,** 2039 (1995); and of related catalysts: *eidem, J. Am. Chem. Soc.* **118,** 100 (1996). Ring-closing metathesis intoduction of carbon-carbon crosslinks in peptides: S. J. Miller *et al., ibid.* 9606. Mechanism of ring-opening metathesis: J. A. Tallarico *et al., ibid.* **119,** 7157 (1997). Yne-ene cross metathesis: M. Schuster, S. Blechert, *Tetrahedron Lett.* **39,** 2295 (1998). Review of use and prepn: A. Fürstner, *Angew. Chem. Int. Ed.* **39,** 3012-3043 (2000).



Purple air-stable microcrystalline solid.

USE: Catalysis of olefin metathesis including ring-closing of dienes, cross metathesis and ring-opening methathesis polymerizations (ROMP).

4551. Grundmann's Ketone. [66251-18-1] (1*R*,3a*R*,7a*R*)-1-[(1*R*)-1,5-Dimethylhexyl]octahydro-7a-methyl-4*H*-inden-4-one; (1*R*,3a*R*,7a*R*)-7a-methyl-1-((*R*)-6-methylheptan-2-yl)-octahydroinden-4-one; Windaus-Grundmann ketone. $C_{18}H_{32}O$; mol wt 264.45. C 81.75%, H 12.20%, O 6.05%. Prepd by ozonolysis of vitamin D_3, *q.v.* Preparative method: A. Windaus, W. Grundmann, *Ann.* **524,** 295 (1936). Prepn: H. H. Inhoffen *et al., Ber.* **90,** 664 (1957). Synthetic applications: H. Nemoto *et al., J. Org. Chem.* **51,** 5311 (1986); P. Bovicelli *et al., ibid.* **57,** 5052 (1992); M. C. Clasby, D. Craig, *Synth. Commun.* **24,** 481 (1994); R. R. Sicinski, H. F. DeLuca, *Bioorg. Med. Chem. Lett.* **5,** 159 (1995); W. H. Okamura *et al., J. Org. Chem.* **67,** 1637 (2002).



Colorless oil, $bp_{0.001}$ 115-120°. $[\alpha]_D^{20}$ +8.9°.

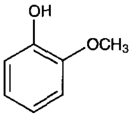
USE: Intermediate in the synthesis of vitamin D active compounds.

4552. Guaiac. [9000-29-7] Gum guaiac; resin guaiac; guaiacum. Resin from ***lignum vitae***, the wood of *Guajacum officinale* L. or *G. sanctum* L., *Zygophyllaceae*. *Constit.* About 70% α- and β-guaiaconic acids, about 11% guaiacic acid, related compds and guaiaretic acid, 15% vanillin, guaiac yellow, guaiac saponin (guaiacin). Use as clinical reagent for occult blood: R. H. Wilkinson, W. A. F. Penfold, *Lancet* **2,** 847 (1969). Acute toxicity: P. M. Jenner *et al., Food Cosmet. Toxicol.* **2,** 327 (1964).

Brown or greenish-brown, irregular lumps. mp 85-90°. Insol in water. Freely sol in alcohol, chloroform, ether, creosote, soln of chloral hydrate, alkalies; slightly sol in benzene, carbon disulfide. LD_{50} orally in rats: >5000 mg/kg (Jenner).

USE: Clinical reagent (blood or hemoglobin).

4553. Guaiacol. [90-05-1] 2-Methoxyphenol; methylcatechol; *o*-hydroxyanisole; 1-hydroxy-2-methoxybenzene; Anastil. $C_7H_8O_2$; mol wt 124.14. C 67.73%, H 6.50%, O 25.78%. Isolated from guaiac resin: Sobrero, *Ann.* **48,** 19 (1843); from hardwood tar: McGinness *et al., Tappi* **43,** 1027 (1960). Prepd by mercuric oxide oxidation of lignin: Lewis, Pearl, **US 2433227** (1947 to Sulphite Prod.); by oxidation of anisole with trifluoroperoxyacetic acid: McClure, Williams, *J. Org. Chem.* **27,** 627 (1962); from acetovanillone + $ZnCl_2$: Read, **US 3057927** (1962 to Ontario Res. Found.); from the diazonium salt of *o*-anisidine: Herbst, **DE 1148236** (1963 to Hoechst). Toxicity data: Taylor *et al., Toxicol. Appl. Pharmacol.* **6,** 378 (1964).



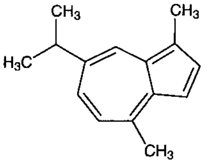
White or slightly yellow cryst mass or colorless to yellowish, very refractive liquid; characteristic odor. Darkens on exposure to air and light. d (crystals) 1.129; d (liq) ~1.112. Solidif 28°, but may remain liq for a long time even at a much lower temp. bp 204-206°; bp_4 53-55°. One gram dissolves in 60-70 ml water, 1 ml glycerol; miscible with alcohol, chloroform, ether, oils, glacial acetic acid. Slightly sol in petr ether; sol in NaOH soln; with moderately concd KOH it forms a sparingly sol compd. *Protect from light.* LD_{50} orally in rats: 725 mg/kg (Taylor).

Phenylacetate. [4112-89-4] Gujaphenyl; Gunyl. $C_{15}H_{14}O_3$; mol wt 242.27.

THERAP CAT: Expectorant.

THERAP CAT (VET): Expectorant.

4554. Guaiazulene. [489-84-9] 1,4-Dimethyl-7-(1-methylethyl)azulene; 7-isopropyl-1,4-dimethylazulene; *S*-guaiazulene; AZ 8; AZ 8 Beris; Eucazulen; Kessazulen; Vaumigan. $C_{15}H_{18}$; mol wt 198.30. C 90.85%, H 9.15%. Isoln from chamomile oil: Sorm *et al., Collect. Czech. Chem. Commun.* **16,** 626 (1951); from guaiac wood oil: Joos, **CH 314487** (1956), *C.A.* **52,** 443b (1958). Total synthesis: Plattner *et al., Helv. Chim. Acta* **32,** 2452 (1949); Sorm *et al., Collect. Czech. Chem. Commun.* **16,** 168 (1951); Jacob *et al., Tetrahedron* **20,** 2821 (1964); J. Mukherjee *et al., J. Am. Chem. Soc.* **101,** 251 (1979). Pharmacokinetics of guaiazulene soluble in animals: H. Mukai *et al., J. Pharmacobio-Dyn.* **8,** 329, 337 (1985). Effect on gastric and duodenal ulcers in rats: S. Okabe *et al., Nippon Yakurigaku Zasshi* **88,** 467 (1986), *C.A.* **106,** 43769 (1987).



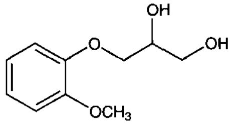
Blue oil. bp_{10} 165-170°.

3-Sulfonate sodium salt. [6223-35-4] 5-Isopropyl-3,8-dimethyl-1-azulenesulfonic acid sodium salt; sodium gualenate; guaiazulene soluble; Azulon. $C_{15}H_{17}NaO_3S$; mol wt 300.35.

Trinitrobenzene deriv. [4968-29-0] $C_{15}H_{18}.C_6H_3N_3O_6$. Violet to black needles from ethanol, mp 151°.

THERAP CAT: Anti-inflammatory; antiulcerative.

4555. Guaifenesin. [93-14-1] 3-(2-Methoxyphenoxy)-1,2-propanediol; glycerol mono(2-methoxyphenyl) ether; glycerol α-(2-methoxyphenyl) ether; guaiacyl glyceryl ether; glyceryl guaiacyl ether; glycerol guaiacolate; α-glyceryl guaiacol ether; *o*-methoxyphenyl glyceryl ether; 1,2-dihydroxy-3-(2-methoxyphenoxy)propane; guaiacol glyceryl ether; guaiphenesin; guaiacuran; MY-301; XL-90; Colrex; Mucinex; Myoscain; Relaxil G; Resyl; Robitussin. $C_{10}H_{14}O_4$; mol wt 198.22. C 60.59%, H 7.12%, O 32.29%. Centrally acting muscle relaxant with expectorant properties. Prepn: Marle, *J. Chem. Soc.* **101,** 305 (1912); Yale *et al., J. Am. Chem. Soc.* **72,** 3710 (1950); Roviralta, Astoul, **ES 212920** (1954), *C.A.* **49,** 8332b (1955). Prepn from 2-methoxyphenol and glycidol: W. Merk *et al.,* **DE 3106995**; *eidem,* **US 4390732** (1982, 1983 to Degussa AG). GLC determn in blood: W. R. Maynard, R. B. Bruce, *J. Pharm. Sci.* **59,** 1346 (1970). Clinical use in chronic respiratory disease: D. G. Workman *et al., Curr. Ther. Res.* **7,** 665 (1965). Clinical efficacy as antitussive: J. J. Kuhn *et al., Chest* **82,** 713 (1982). Pharmacokinetics and cardiopulmonary effects in horses: J. A. E. Hubbell *et al., Am. J. Vet. Res.* **41,** 1751 (1980). Use in equine anesthesia: J. L. Grandy, W. N. McDonell, *J. Am. Vet. Med. Assoc.* **176,** 619 (1980); G. J. Brouwer, *Equine Vet. J.* **17,** 133 (1985).



Minute rhombic prisms from ether, mp 78.5-79°. bp_{19} 215°. Slightly bitter aromatic taste. One gram dissolves in 20 ml water at 25°. Much more sol in hot water; freely sol in ethanol; sol in chloroform, glycerol, propylene glycol, DMF; moderately sol in benzene. Practically insol in petr ether.

THERAP CAT: Expectorant

THERAP CAT (VET): Expectorant; muscle relaxant.

4556. Guaiol. [489-86-1] [3*S*-(3α,5α,8α)]-1,2,3,4,5,6,7,8-Octahydro-α,α,3,8-tetramethyl-5-azulenemethanol; 3,8-dimethyl-5-(α-hydroxyisopropyl)-Δ^9-octahydroazulene; champaca camphor; champacol; guaiac alcohol; Guajol. $C_{15}H_{26}O$; mol wt 222.37. C 81.02%, H 11.79%, O 7.19%. A sesquiterpene alc from guaiac wood: *Michelia champaca* L., *Magnoliaceae:* also from oil of wood of *Bulnesia sarmienti* Lorentz, *Zygophyllaceae.* Isoln: Plattner, Lemay, *Helv. Chim. Acta* **23,** 897 (1940). Structure: Plattner, Magyar, *ibid.* **25,** 581 (1942). Stereochemistry: Takeda, Minato, *Tetrahedron Lett.* **1960** (22), 33; Minato, *Chem. Pharm. Bull.* **9,** 625 (1961); *idem, Tetrahedron* **18,** 365 (1962). Total synthesis of *dl*-form: Buchanan, Young, *Chem. Commun.* **1971,** 643; *eidem, J. Chem. Soc. Perkin Trans. I* **1973,** 2404; Marshall *et al., Tetrahedron Lett.* **1971,** 885; Marshall, Greene, *J. Org. Chem.* **37,** 982 (1972); Andersen, Uh, *Tetrahedron Lett.* **1973,** 2079.