

THE MERCK INDEX

AN ENCYCLOPEDIA OF
CHEMICALS, DRUGS, AND BIOLOGICALS

FOURTEENTH EDITION

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Cystatin B. [99194-04-4] Stefin B; CPI-B; NCPI; neutral cysteine proteinase inhibitor. Broadly distributed in human cells and tissues; general cytosolic inhibitor to protect against leakage of lysosomal enzymes. Mutations in the cystatin B gene have been associated with progressive myoclonus epilepsy. Isolin from human spleen: M. Järvinen, A. Rinne, *Biochim. Biophys. Acta* **708**, 210 (1982); from human liver: G. D. J. Green et al., *Biochem. J.* **218**, 939 (1984). Review of role in Unverricht-Lundborg disease: A.-E. Lehesjoki, *EMBO J.* **22**, 3473-3478 (2003). Mature human form is a single chain, non-glycosylated peptide containing 98 amino acid residues; mol wt 11.2 kDa. Isoelectric point: 5.6-6.3.

Cystatin C. [91448-99-6] Post- γ -globulin; γ -CSF; γ -trace. Found ubiquitously in vertebrates; major extracellular cysteine peptidase inhibitor in mammals. Isolin from human CSF: J. Clausen, *Proc. Soc. Exp. Biol. Med.* **107**, 170 (1961); from urine of patients with renal dysfunction: E. A. Butler, F. V. Flynn, *J. Clin. Pathol.* **14**, 172 (1961). Identification as a cystatin: A. J. Barrett et al., *Biochem. Biophys. Res. Commun.* **120**, 631 (1984). Review of biochemistry and clinical role: M. Mussap, M. Plebani, *Crit. Rev. Clin. Lab. Sci.* **41**, 467-550 (2004); of efficacy as biomarker for glomerular filtration rate: G. Filler et al., *Clin. Biochem.* **38**, 1-8 (2005). Clinical evaluation to predict risk of cardiovascular events in elderly patients: M. G. Shlipak et al., *N. Engl. J. Med.* **352**, 2049 (2005). Mature human form is a single chain, non-glycosylated peptide containing 120 amino acid residues; mol wt 13.3 kDa. Isoelectric point: 9.3. Electrophoretic mobility: γ_3 (agarose gel electrophoresis at pH 8.6). $E_{1\text{cm}}^{1\%}$ 9.1 (280 nm). Conc in plasma of healthy adults: 0.8 to 1.2 mg/l.

Therap Cat: Cystatin C as diagnostic aid (renal function).

2779. Cysteamine. [60-23-1] 2-Aminoethanethiol; mercaptamine; β -mercaptoethylamine; 2-aminoethyl mercaptan; thioethanolamine; decarboxycysteine; MEA; mercamine; L-1573; B-captan; Lambratene (formerly). C_2H_7NS ; mol wt 77.15. C 31.14%, H 9.15%, N 18.16%, S 41.56%. $HSCH_2CH_2NH_2$. A sulfhydryl compound with a variety of biological effects. Prep: Gabriel, Leupold, *Ber.* **31**, 2837 (1898); Knorr, Rössler, *ibid.* **36**, 1281 (1903); Mills, Jr., Bogart, *J. Am. Chem. Soc.* **62**, 1173 (1940); Wenker, *ibid.* **57**, 2328 (1935); D. A. Shirley, *Preparation of Organic Intermediates* (Wiley, New York, 1951) p 189. Use in treatment of paracetamol (acetaminophen) poisoning: L. F. Prescott et al., *Lancet* **2**, 109 (1976); A. L. Harris, *Br. Med. J.* **284**, 825 (1982). Effects in nephropathic cystinosis: M. Yudkoff et al., *N. Engl. J. Med.* **304**, 141 (1981). Radioprotective effects: R. P. Bird, *Radiat. Res.* **72**, 290 (1980); C. J. Koch, R. L. Howell, *ibid.* **87**, 265 (1981). Cysteamine has been shown to be a duodenal ulcerogen in rats: H. Selye, S. Szabo, *Nature* **244**, 458 (1973); S. Szabo, *Am. J. Pathol.* **93**, 273 (1978); P. Kirkegaard et al., *Scand. J. Gastroenterol.* **15**, 621 (1980). Review: S. Szabo, *Lab. Invest.* **51**, 121 (1984). It has also been found to deplete somatostatin concentration: S. Szabo, S. Reichlein, *Endocrinology* **109**, 2255 (1981); S. M. Sagar et al., *J. Neurosci.* **2**, 225 (1982). In pituitary tissue, cysteamine is a potent depletor of prolactin concentrations *in vivo* and *in vitro*: W. J. Millard et al., *Science* **217**, 452 (1982). Toxicity studies: E. Beccari et al., *Arzneim.-Forsch.* **5**, 421 (1955); D. L. Klayman et al., *J. Med. Chem.* **12**, 510 (1969); P. K. Srivastava, L. Field, *ibid.* **18**, 798 (1975).

Crystals by sublimation *in vacuo*. Disagreeable odor. mp 97-98.5°. Oxidizes to cystamine on standing in air. Freely sol in water, alkaline reaction. LD₅₀ in mice (mg/kg): 625 orally; 250 i.p. (Klayman); (Srivastava, Field).

Hydrochloride. $C_2H_7NS.HCl$. Crystals from alc, mp 70.2-70.7°. Sol in water, alcohol. LD₅₀ (cg/kg): 23.19 i.p. in rats; 14.95 i.v. in rabbits (Beccari).

USE: Experimentally as a radioprotective agent and to produce acute and chronic duodenal ulcers in rats.

Therap Cat: Antidote to acetaminophen.

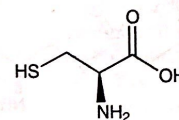
2780. Cysteic Acid. [13100-82-8] 3-Sulfoalanine; α -amino- β -sulfopropionic acid. $C_3H_7NO_5S$; mol wt 169.16. C 21.30%, H 4.17%, N 8.28%, O 47.29%, S 18.96%. $HOOCCH(NH_2)CH_2SO_3H$. Has been isolated from human hair oxidized with permanganate: Lissizin, *Z. Physiol. Chem.* **173**, 309 (1928). Occurs normally in the outer part of the sheep's fleece, where the wool is exposed to light and weather: Martin, Syngé, *Adv. Protein Chem.* **2**,

3 (1945). Prep'd from cystine or cysteine by oxidation with bromine in water: Friedmann, *Beitr. Chem. Physiol. Pathol.* **3**, 25, 38; Gortner, Hoffman, *J. Biol. Chem.* **72**, 435 (1927).

L-Form. Octahedra or needles from dil alc (also forms a monohydrate, prismatic needles). When anhydr, dec 260°. $[\alpha]_D^{20} +8.66^\circ$ (1.85 g in 25 ml). pKa₁ (25°): 1.89; pKa₂ 8.7; pKb about 12.7. Soluble in water. Insol in alcohol.

DL-Form. Crystals, dec 245°.

2781. Cysteine. [52-90-4] L-Cysteine; Cys; C; β -mercaptoalanine; (R)-2-amino-3-mercaptopropanoic acid; 2-amino-3-mercaptopropionic acid; α -amino- β -thiolpropionic acid; half-cystine; thioserine. $C_3H_7NO_2S$; mol wt 121.16. C 29.74%, H 5.82%, N 11.56%, O 26.41%, S 26.47%. A non-essential amino acid in human development. Readily oxidizes to form a dimeric amino acid, cystine, *q.v.*, in which the two Cys are linked via a disulfide bridge, a common structural feature in proteins. 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 vol 1-3* (John Wiley and Sons, Inc., New York, 1961) pp. 1879-1928, *passim*. Simple synthesis of racemic cysteine: V. J. Martens et al., *Angew. Chem. Int. Ed.* **20**, 668 (1981). Determination in proteins: J. G. Hoogerheide, C. M. Campbell, *Anal. Biochem.* **201**, 146 (1992); D. Atherton et al., *ibid.* **212**, 98 (1993). Review of biosynthesis: N. M. Kredich et al., *Ciba Found. Symp.* (Netherlands) **72**, 87-99 (1980). Review of transport in mammalian cells: S. Bannai, *Biochim. Biophys. Acta* **779**, 289-306 (1984). Review of effects on acrylonitrile toxicity: D. E. Nerland et al., *Drug Metab. Rev.* **20**, 233-246 (1989). Review of thermodynamics and kinetics: T. R. Ralph et al., *J. Electroanal. Chem.* **375**, 1-15 (1994); of electrosynthesis: *eidem, ibid.* 17-27. Review of role in chemo- and radioprotectant strategies: J. C. Roberts, *Amino Acids* **8**, 113-124 (1995).



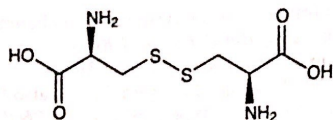
Crystals. $[\alpha]_D^{25} +6.5^\circ$ (5N HCl); $[\alpha]_D^{25} +13.0^\circ$ (glacial acetic acid). pK₁ 1.71; pK₂ 8.33; pK₃ 10.78. Absorption spectrum: Abderhalden, Rossner, *Z. Physiol. Chem.* **178**, 160 (1928). Freely sol in water, alcohol, acetic acid, ammonia water. Insol in ether, acetone, ethyl acetate, benzene, carbon disulfide, carbon tetrachloride. In neutral or slightly alkaline aq solns it is oxidized to cystine by air. More stable in acidic solns.

Hydrochloride. [52-89-1] $C_3H_7NO_2S.HCl$. Crystals, dec 175-178°. $[\alpha]_D^{25} +5.0^\circ$ (5N HCl); $[\alpha]_D^{25} +10.0^\circ$ (glacial acetic acid). Sol in water, alcohol, acetone; the aq soln is acid. *Keep tightly closed.* Decomposes and oxidizes slowly; hygroscopic.

USE: As dough conditioner.

Therap Cat (VET): Has been used as a detoxicant.

2782. Cystine. [56-89-3] L-Cystine; [R-(R*,R*)]-3,3'-dithiobis[2-aminopropanoic acid]; dicysteine; β,β' -dithiodialanine; α -diamino- β -dithiolactic acid; β,β' -diamino- β,β' -dicarboxydiethyl disulfide; bis(β -amino- β -carboxyethyl) disulfide; Gelucystine. $C_6H_{12}N_2O_4S_2$; mol wt 240.30. C 29.99%, H 5.03%, N 11.66%, O 26.63%, S 26.69%. Non-essential amino acid for human development. Formed by the dimerization of two cysteines, *q.v.* through the sulfur. These disulfide bridges occur both within and between polypeptides; often found in extracellular proteins. First amino acid described in 1810 by Wollaston. Isolin from horn hydrolysate: K. A. H. Mörmner, *Z. Physiol. Chem.* **28**, 595 (1899). 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. 1879-1928, *passim*. Distribution in protein: R. C. Fahey et al., *J. Mol. Evol.* **10**, 155 (1977). Review of lysosomal transport including pathophysiology: W. Gahl in *Pathophysiol. Lysosomal Transp.*, J. G. Thoene, Ed. (CRC Press, Boca Raton, FL, 1992) pp 45-71. Review of thermodynamics and kinetics: T. R. Ralph et al., *J. Electroanal. Chem.* **375**, 1-15 (1994); of electrosynthesis: *eidem, ibid.* 17-27.



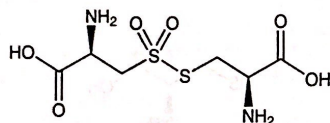
Hexagonal tablets from water, dec 260-261° (sealed tube). $[\alpha]_D^{20}$ -223.4° (1.0N HCl). pK_1 1; pK_2 2.1; pK_3 8.02; pK_4 8.71 at 35°. Soly in water (g/l) at 25°: 0.112; at 50°: 0.239; at 75°: 0.523; at 100°: 1.142. Quite sol in aq solns below pH 2 or above pH 8. Soly curves: Sano, *Biochem. Z.* **168**, 14 (1926). Insol in alc. Absorption spectrum: Marchlewski, Nowotonowna, *Bull. Soc. Chim. Fr.* [4] **39**, 163, 166 (1926).

D-Form. [349-46-2] Crystals. $[\alpha]_D^{20}$ +223° (1.0N HCl). Soly in water at 25°: 0.057 g/l.

DL-Form. [923-32-0] Crystals. Soly in water at 25°: 0.057 g/l.

meso-Form. [6020-39-9] Crystals. Soly in water: 0.056 g/l.

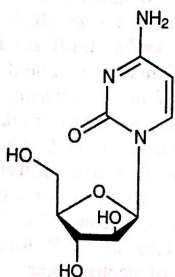
2783. L-Cystine S,S-Dioxide. [30452-69-8] 2-Amino-2-carboxyethyl 2-amino-2-carboxyethanethiosulfonate; L-cystine thiosulfonate; sacysyl-cysteine. $C_6H_{12}N_2O_6S_2$; mol wt 272.30. C 26.47%, H 4.44%, N 10.29%, O 35.25%, S 23.55%. Oxidation product of cystine. Prepn: G. Toennies, T. F. Lavine, *J. Biol. Chem.* **113**, 571 (1936); R. Emilozzi, L. Pichat, *Bull. Soc. Chim. Fr.* **1959**, 1887. Originally thought to be a mixture of two isomers, cystine S,S-dioxide and *cystine S,S'-dioxide*: G. E. Utzinger, *Experientia* **17**, 374 (1961). Elucidation of structures: G. Axelson *et al.*, *Spectrochim. Acta* **23A**, 2015 (1967); L. D. Setiawan *et al.*, *Surf. Interface Anal.* **7**, 188 (1985). Use in deternm of sulfite: T. Ubuka *et al.*, *Anal. Biochem.* **126**, 273 (1982); *idem et al.*, *ibid.* **140**, 449 (1984).



Solid, relatively unstable in aqueous solns; disproportionates to cystine and cysteine sulfinic acid.

USE: In detection of sulfites and thiosulfate.

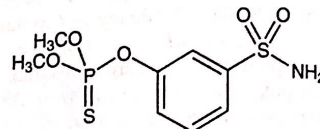
2784. Cytarabine. [147-94-4] 4-Amino-1-β-D-arabinofuranosyl-2(1H)-pyrimidinone; 1-β-D-arabinofuranosylcytosine; Ara-C; β-cytosine arabinoside; aracytidine; CHX-3311; U-19920; Alexan; Aracytine; Cytosar; Depocyte; Udicil. $C_9H_{13}N_3O_5$; mol wt 243.22. C 44.44%, H 5.39%, N 17.28%, O 32.89%. Nucleoside analog; converted by cellular kinases into the active metabolite, *AraCTP*. Prepn: J. H. Hunter, *US 3116282* (1963 to Upjohn); T. Y. Shen *et al.*, *J. Org. Chem.* **30**, 835 (1965). NMR soln structure of Ara-C within a DNA dodecamer: B. I. Schweitzer *et al.*, *Biochemistry* **33**, 11460 (1994). Crystal structure of complex with human topoisomerase I: J. E. Chrencik *et al.*, *J. Biol. Chem.* **278**, 12461 (2003). Clinical pharmacology and toxicology: R. C. Donehower *et al.*, *Cancer Treat. Rep.* **70**, 1059 (1986). Symposium on clinical pharmacology, pharmacokinetics and efficacy in leukemia: *Scand. J. Haematol.* **36**, Suppl. 44, 1-74 (1986). Review of development of a high dose treatment for acute myeloid leukemia: R. L. Capizzi, *Invest. New Drugs* **14**, 249-256 (1996); of cellular metabolism and mechanism of action: S. Grant, *Adv. Cancer Res.* **72**, 197-233 (1998).



Crystals from ethanol, mp 212-213°. $[\alpha]_D^{24}$ +153° (c = 0.5 in water). uv max at pH 2: 281.0, 212.5 nm (ε 13171, 10230); at pH 12: 272.5 nm (ε 9259).

THERAP CAT: Antineoplastic.

2785. Cythioate. [115-93-5] Phosphorothioic acid O-[4-(aminosulfonyl)phenyl] O,O-dimethyl ester; phosphorothioic acid O,O-dimethyl ester O-ester with p-hydroxybenzenesulfonamide; O,O-dimethyl O-p-sulfamoylphenylphosphorothioate; CL-26691; ENT-25640; Proban. $C_8H_{12}NO_5PS_2$; mol wt 297.29. C 32.32%, H 4.07%, N 4.71%, O 26.91%, P 10.42%, S 21.57%. Prepn: G. Berkelhammer, *US 3005004* and R. I. Hewitt, G. Berkelhammer, *US 3179560* (1961, 1965 to Am. Cyanamid). Pharmacodynamics: H. G. Smith, R. L. Goulding, *J. Econ. Entomol.* **63**, 1640 (1970). Efficacy as ectoparasiticide: C. P. Doval, I. Gupta, *Indian Vet. J.* **55**, 890 (1978); P. M. Bowen, N. J. Caldwell, *Vet. Med. Small Anim. Clin.* **77**, 79 (1982). Toxicity data: E. E. Kenaga, W. E. Allison, *Bull. Entomol. Soc. Am.* **15**, 85 (1969).

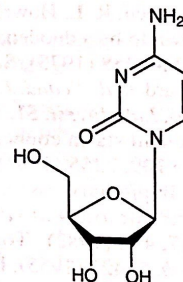


Crystals, mp 70-71°. n_D^{25} 1.5346. LD₅₀ orally in rats: 160 mg/kg (Kenaga, Allison).

USE: Insecticide.

THERAP CAT (VET): Ectoparasiticide.

2786. Cytidine. [65-46-3] 4-Amino-1-β-D-ribofuranosyl-2-(1H)-pyrimidinone; cytosine riboside; 1-β-D-ribofuranosylcytosine. $C_9H_{13}N_3O_5$; mol wt 243.22. C 44.44%, H 5.39%, N 17.28%, O 32.89%. Constituent of nucleic acids. Isoln from yeast nucleic acid: Levene, Jacobs, *Ber.* **43**, 3154 (1910); Levene, La Forge, *ibid.* **45**, 608 (1912). Sepn from other nucleosides by ion-exchange chromatography: Cohn in Chargaff-Davidson, *The Nucleic Acids vol. I* (New York, 1955) p 211. Synthesis: Howard *et al.*, *J. Chem. Soc.* **1947**, 1052. Crystal structure: Furberg *et al.*, *Acta Crystallogr.* **18**, 313 (1965). Review: *Basic Principles in Nucleic Acid Chemistry vol. 1*, P. O. P. Ts'o, Ed. (Academic Press, New York, 1974) *passim*.



Long needles from 90% ethanol, dec 220-230°. $[\alpha]_D^{25}$ +31° (c = 0.7 in water). Freely sol in water, less sol in alcohol. pK (amino, cationic) 4.22; pK (sugar, anionic) 12.5. uv max (pH 8.2): 271 nm (ε 9100); (pH 2.2): 280 nm (ε 13400), Voet *et al.*, *Biopolymers* **1**, 193 (1963).

Sulfate. $(C_9H_{13}N_3O_5)_2 \cdot H_2SO_4$. Long prismatic needles, mp 224-225° (dec with effervescence). $[\alpha]_{589}^{25}$ +34°; $[\alpha]_{546}^{25}$ +43°.

2787. 2'-Cytidylic Acid. [85-94-9] Cytidine-2'-monophosphate; cytidylic acid α; 2'-cytidinephosphoric acid; cytidine-2'-phosphate; 2'-cytosylic acid; 2'-CMP. $C_9H_{14}N_3O_8P$; mol wt 323.20. C 33.45%, H 4.37%, N 13.00%, O 39.60%, P 9.58%. Ribonucleic acid inhibitor. Prepn from yeast ribonucleic acid: Cohn, Carter, *J. Am. Chem. Soc.* **72**, 2606 (1950); Loring *et al.*, *J. Biol. Chem.* **196**, 807 (1952); by phosphorylation of N⁶,O^{3'},O^{5'}-tribenzoylcytidine: Rammner, Khorana, *J. Am. Chem. Soc.* **84**, 3112 (1962). Crystal structure and conformation of the trihydrate: Kartha *et al.*, *Science* **179**, 495 (1973). Reviews: See Cytidine.