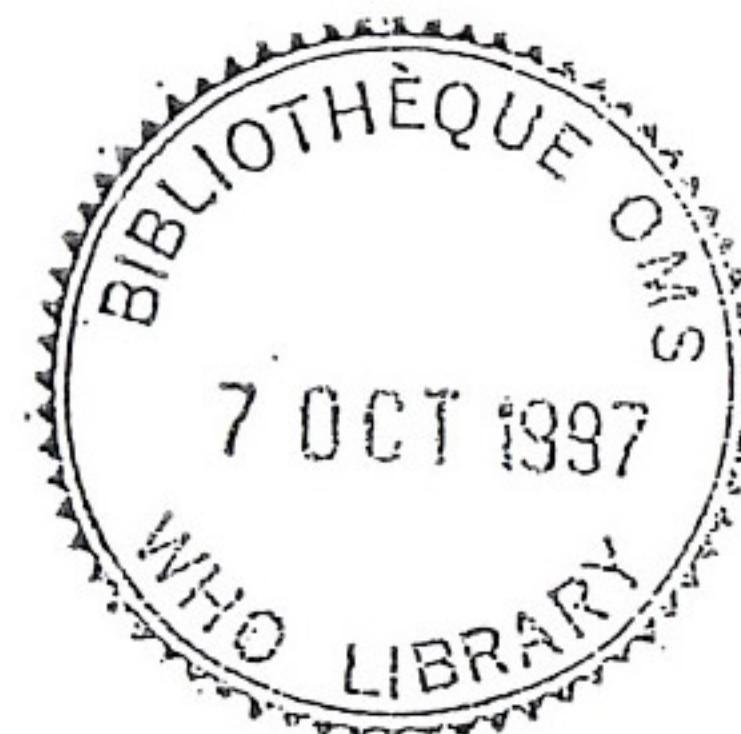


# THE MERCK INDEX

AN ENCYCLOPEDIA OF  
CHEMICALS, DRUGS, AND BIOLOGICALS

TWELFTH EDITION



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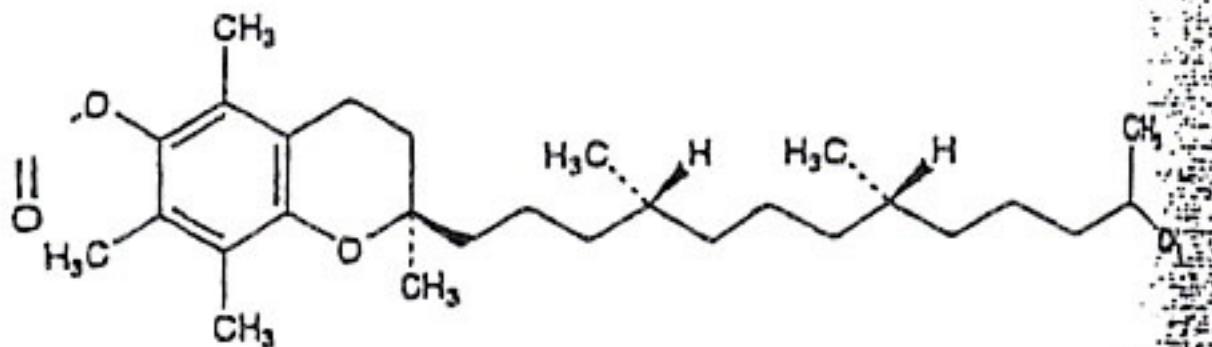
## Voacamine

10168

30-220°;  $n_D^{25}$  1.5045. uv max: 294 nm ( $E_{1\text{cm}}^{1\%}$  71). ally insol in water. Freely sol in oils, fats, acetone, chloroform, ether, other fat solvents. Stable to heat in the absence of oxygen. Not affected by acid 100°. Slowly oxidized by atm oxygen, rapidly by silver salts. Gradually darkens on exposure.

As an antioxidant in vegetable oils and shortenings. THERAP CAT: Treatment of vitamin E deficiency. THERAP CAT (VET): Nutritional factor. Interrelations with selenium. (Prevents muscle degeneration, also encelaria and exudative diathesis.) Has been used to increase fertility.

60. Vitamin E Acetate.  $[2R^*(4R^*,8R^*)]_3,4-Dihydro-5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-1,2,5,6-ol acetate$ ; 2,5,7,8-tetramethyl-2-(4,8,12-trimethyl)-6-chromanol acetate;  $\alpha$ -tocopherol acetate;  $\gamma$ -tocopheryl acetate;  $C_{31}H_{52}O_3$ ; mol wt 472.75. C 78.76%, H 10.15%. Prepn from *dl*- $\alpha$ -tocopherol and acetic anhydride: Surmatis, Weber, U.S. pat. 2,723,278 (1955); J. Am. Chem. Soc. 84, 3196 (1962). Stereochemical synthesis: K.-K. Chan et al., J. Org. Chem. 43, 3435 (1978). Synthesis of all eight stereoisomers: N. Cohen, Chim. Acta 64, 1158 (1981). Comprehensive review: B. C. Rudy, B. Z. Senkowski, Anal. Profiles 3, 111-126 (1974).



*l*-Form, Detulin, Ephynal, Eprolin, Epsilon-M, Epsilon-imin, Evion, Juvela, OptoVit-E, Toco 500, Vitagull. Low, viscous liquid; mp -27.5°.  $d_4^{21.3}$  0.9533. bp<sub>0.5</sub> 194°; bp<sub>0.3</sub> 224°.  $n_D^{20}$  1.4950-1.4972. uv max (ethane): 285.5 nm. Practically insol in water. Freely sol in acetone, chloroform, ether. Less readily sol in alc. Unlike free vitamins, the acetate is practically unaffected by oxidizing influence of air, light, and ultraviolet light. *l*-Form.  $[2R-[2R^*(4R^*,8R^*)]]_3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6-ol$ , *E*-Vicotrat, Spondyvit, Tocopherex. Crystals; mp 22° +0.25° (c = 10 in chloroform);  $[\alpha]_D^{25} +3.2^\circ$  (in ethanol). *D*-Form, crystals, mp 23°.  $[\alpha]_D^{25} -2.0^\circ$  (in ethanol). Note: The international unit of vitamin E is equal to one mg of standard *dl*- $\alpha$ -tocopheryl-acetate. The *d*-form is more active: 1 mg = 1.36 I.U. *l*- $\alpha$ -Tocopheryl acetate has 42% the activity of *d*- $\alpha$ -tocopheryl acetate in the rat hemolysis test. Based on this activity a potency ratio of 1.4:1 for *d*- $\alpha$ -tocopheryl acetate compared to *dl*- $\alpha$ -tocopheryl acetate has been established.

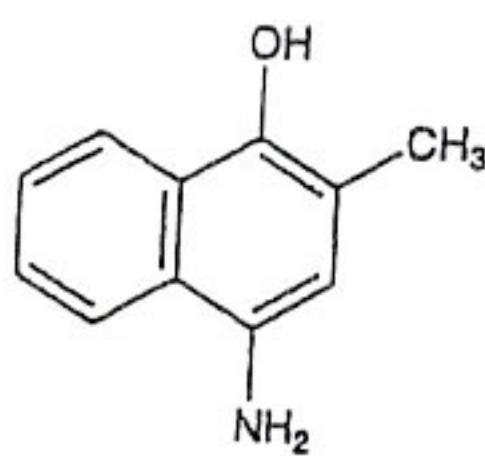
THERAP CAT: Vitamin.

THERAP CAT (VET): Vitamin.

1. Vitamin K. General term referring to a group of quinone derivatives required for the bioactivation of proteins involved in hemostasis. The designation "K" was derived from the German "Koagulationsvitamin." Vitamins K compds are classified into 3 groups: phylloquinone (K<sub>1</sub>), g.v., found in green plants; menaquinones (K<sub>2</sub>), g.v., primarily produced by intestinal bacteria; and menadione (K<sub>3</sub>), g.v., and derivatives which are synthetic, lipid soluble compounds. Reduced in vivo to dihydrovitamin K (KH<sub>2</sub>) which serves as a coenzyme in the conversion of glutamic acid residues to  $\gamma$ -carboxyglutamic acid (Gla), g.v., in the post-translational modification of blood coagulation factors VII, IX and X, g.v., and the anticoagulant proteins C and S. Other Gla-containing proteins, such as the bone matrix protein, osteocalcin, g.v., have been identified in a wide variety of tissues. This  $\gamma$ -carboxylation is accompanied by oxidation of KH<sub>2</sub> to vitamin K epoxide which is then reduced back to vitamin K. Discovery: H. Dam, Biochem. 215, 475 (1929); 220, 158 (1930); Nature 135, 652 (1936); Historical survey: H. Dam, Vit. Horm. 24, 295-306 (1952). Menadione and phylloquinone are metabolized by

10 menaquinone-4: C. Martius, H. O. Esse: *Vitamin* 331, 1 (1958); H. H. W. Thijssen, M. J. Driessens, Brit. J. Nutr. 72, 415 (1994). Comprehensive review: Friedrich in *Vitamins* (de Gruyter, New York) 285-338. Review of metabolism and role in nutrition: M. J. Shearer, Blood Rev. 6, 92-104 (1992); Suttie, J. Am. Diet. Assoc. 92, 585-590 (1992); of action: P. Dowd et al., Nat. Prod. Rep. 11, 1517 (1994); of pharmacology and therapeutic use: P. Dowd et al., Drugs 49, 376-387 (1995). Physiological actions: J. Shearer, Lancet 345, 229-234 (1995).

10162. Vitamin K<sub>5</sub>. 4-Amino-2-methyl-1-(4-amino-2-methyl-1-naphthol)-1-hydroxy-2-methyl-naphthalene; 2-methyl-4-amino-1-hydroxynaphthalene; 3-methyl-4-hydroxymethylamine; Synkamin.  $C_{11}H_{11}NO$ ; mol wt 162.28%, H 6.40%, N 8.09%, O 9.24%. Prepd from naphthalene or from menadione: Sah, Rec. Trav. 458 (1940); 60, 373 (1941); Veldstra, Wiardi, (1942); 62, 75 (1943). Use as food preservative: Steele, Food Technol. 12, 501 (1958).

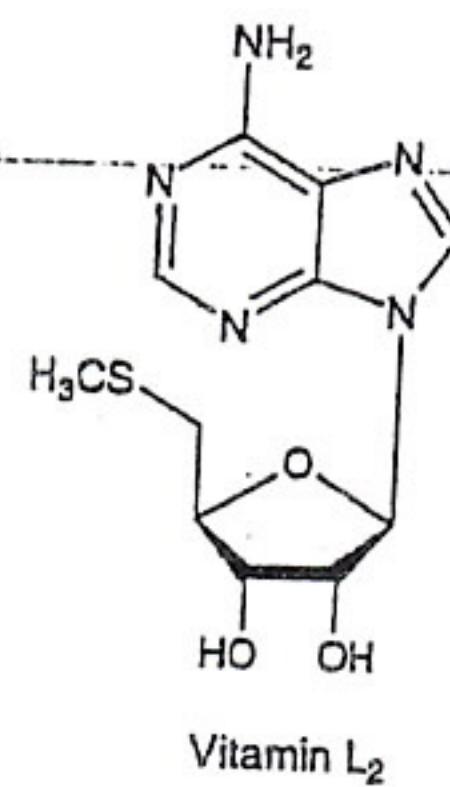


Hydrochloride,  $C_{11}H_{11}NO \cdot HCl$ , Kayvisyn. 1 dil HCl, darkens at 262°, dec 280-282°. Turns violet on exposure to air and light. Freely sol in alc. Insol in ether. N-Acetyl analog,  $C_{13}H_{13}NO_2$ , 4-acetamido-naphthalene, K-Vitrat. Needles, mp 208-210°.

USE: Food preservative.

THERAP CAT: Vitamin (prothrombogenic).

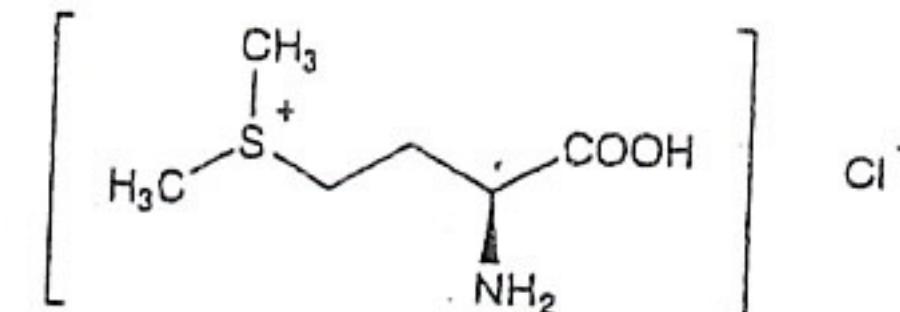
10163. Vitamin(s) L. Factors presumably necessary for lactation. Vitamin L<sub>1</sub>: See o-Aminobenzoic Acid. Vitamin L<sub>2</sub> was shown to be 7-[tetrahydro-3,4-dihydroxy-5-(methylmercaptomethyl)-2-furyl]adenine: Nakahara et al., Sci. Papers Inst. Phys. Chem. Research (Tokyo) 40, 433 (1943), 41, 6317c (1947). Manuf: Sato et al., Japan. pats. 244 ('62) and 16,015 ('69), C.A. 59, 1746f (1963) and C.A. 71, 102146j (1972).



10164. Vitamin T. Tegotin; termitin; torutilin; factor T; vitamin T Goetsch; Goetsch's vitamin; Temina. A complex growth-promoting substance, originally obtained from termites: Goetsch, Oesterr. Zool. Z. 1, 58-85 (1946). Also obtainable from roaches, yeasts and fungi. The isoln procedure has never been described. Isoln of "vitamin T complex" from yeast: Koch et al., Ger. pat. 1,000,962 (1957) (to Aschaffenburger Zellstoffwerke), C.A. 54, 18898d (1960). Vitamin T may be a mixture of known vitamins and growth-promoting factors: Koch et al., Naturwiss. 38, 339 (1951). Polemic by Barkow, Goetsch, ibid. 42, 346 (1955).

10165. Vitamin U. (S)-(3-Amino-3-carboxypropyl)-dimethyl sulfonium chloride; methylmethioninesulfonium chloride; MMSC; Cabagin-U; Epadyn-U; Vitas-U.  $C_6H_{14}NO_3S$ ; mol wt 199.70. C 36.09%, H 7.07%, Cl 17.75%, N

7.01%, O 16.02%, S 16.06%. The anti-ulcer vitamin reported in cabbage leaves and other green vegetables: G. Cheney, California Med. 77, 248 (1952). Activity: V. Z. Szabo, G. Vargha, Arzneimittel-Forsch. 10, 23 (1960); K. Seri et al., ibid. 29, 1517 (1979). Prepn: Y. Kanai, Y. Kawamura, Japan. pat. 4757 ('62) (to Nippon Kayaku), C.A. 58, 12672e (1963); H. Wagner, Ger. pat. 1,239,697 (1967 to Degussa), C.A. 67, 73866e (1967).



Needles, mp 134° (dec). LD<sub>50</sub> i.v. in mice: 2760 mg/kg. I.V. Zaikonnikova, L. G. Urazava, C.A. 80, 10388y (1974). Bromide analog,  $C_6H_{14}BrNO_2S$ , methylmethioninesulfonium bromide, Ardésyl. mp 139° (dec).

THERAP CAT: Treatment of gastric disorders.

10166. Vitride. Dihydrobis(2-methoxyethanolato-O,O')aluminate(1-) sodium; sodium bis(2-methoxyethoxy)-aluminum hydride.  $C_6H_{16}AlNaO_4$ ; mol wt 202.16. C 35.65%, H 7.98%, Al 13.35%, Na 11.37%, O 31.66%. NaAl(H<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>)<sub>2</sub>. Prepn: Casensky et al., U.S. pat. 3,507,895 (1970). Properties: Vit, Eastman Organic Chemical Bulletin 42(3), 1 (1970).

Highly viscous liquid at room temp. Miscible in a great variety of inert solvents (e.g., aromatic hydrocarbons and ethers). Immiscible in paraffinic hydrocarbons. Thermally stable at 200°C; thermal decomposition starts at 205°C and is vigorous.

USE: Reducing agent.

in various tissues. Has binding sites for integrin heparin, complement components, and perf. Thought to play a regulatory role in hemostasis, healing, tissue remodeling and cancer. Synt. hepatocytes as a single chain polypeptide, mol wt Binds readily to proteoglycans of the extracellular and is deposited in normal loose connective tissue, elastin fibers, and in the vascular wall. A sized by platelets, macrophages and megakaryocytes released by activated platelets in different multistep process. Promotes cellular attachment, spreading and migration, variety of cell types and serves as a matrix regulator of blood coagulation. Identification: I. J. Cell Biol. 32, 297 (1967). Isoln and comp. fibronectin, g.v.: D. Barnes et al., J. Supramol. St. (1980). Purification and tissue distribution: E. C. et al., Proc. Nat. Acad. Sci. USA 80, 4003 (1983) acid sequence: S. Suzuki et al., EMBO J. 4, 25 Identity with S-protein: K. T. Preissner et al., Biophys. Res. Commun. 134, 951 (1986); B. R. To F. Mosher, Blood 68, 737 (1986). Review of physiological function in hemostasis: K. T. Preissner, Rev. Cell Biol. 7, 275-310 (1991); K. T. Preissner, Thromb. Haemost. 66, 123-132; 189-194 (1991). vitronectin receptors and role in cell growth and division: B. Felding-Habermann, D. A. Cheresh, C. Cell Biol. 5, 864-868 (1993).

10168. Voacamine. 12-Methoxy-13-[3 $\alpha$ ]-17-methoxovobasan-3-yl]ibogamine-18-carboxylic acid mevoacanginine.  $C_{43}H_{52}N_4O_5$ ; mol wt 704.91. C 7.44%, N 7.95%, O 11.35%. Bisindole alkaloid Voacangu africana Stapf., V. thouarsii R. & Sch., (K. Sch.) Pichon and V. schweinfurthii Stapf., Ap. Janot, Goutarel, Compt. Rend. 240, 1719 (1955) Org. Chem. 23, 1455 (1958); Janot, Goutarel, 2,823,204 (1958 to Lab. Gobey). Identity with nine: LeBarre, Gillo, Bull. Acad. Roy. Med. Belg. (1956). Cleaved by acid catalysis to voacangine: Naturwiss. 48, 694 (1961). Structure: Goutarel, Compt. Rend. 243, 1670 (1956); Percheron, An (Paris) 4, 303 (1959); Büchi et al., J. Am. Chem.