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THIRTEENTH EDITION

THE MERCCK INDEX

AN ENCYCLOPEDIA OF
CHEMICALS, DRUGS, AND BIOLOGICALS

THIRTEENTH EDITION

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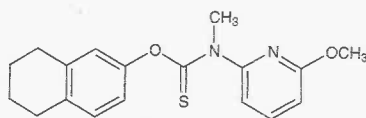
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ap solutes and can interact with cell-carry into cells biologically active normally penetrate the plasma membranes protects these materials from an cultures, from inactivation within atory system or, for pesticides and y rain or irrigation. Liposomes may ole adsorption onto the cell surface, osome is delivered to the lysosomal plasma membrane (liposome content plasm) and lipid exchange between without cell association of liposome used as models in biological memental targeted drug delivery systems ologically active materials. See also and thermodynamics: J. N. Israeophys. *Acta* **470**, 185 (1977). Effect Toffano *et al.*, "Phospholipid Lipopamine Metabolism and on the Sndocrinology: *Biological and Clinical* Macleod, Eds. (Academic Press, New Interaction with nucleic acids: B. Brostruct. *Dyn.* **1**, 1535 (1984). Synthesis ologically active materials: D. P. Pazoka, Jr., **BE 874408** corresp to US for pesticides: *idem*, **US 4241046** ythrocytic malaria by liposomes conds: C. R. Alving *et al.*, *Science* **205**, ology: H. E. Schaeffer, D. L. Krohn, *Sci.* **22**, 220 (1982). In delivery of sperility control: L. Mettler, A. B. Czupr to Nattermann). In transfer of nucle. **2140822** (1984 to Stauffer). In gene: C. Nicolau, *Biochem. Soc. Trans.* **12**, -phospholipid liposomes as drug delivascites tumor in mice: K. R. Patel *et al.*, *Acta* **797**, 20 (1984). Review of early *al.*, *ibid.* **457**, 259-302 (1976); of pharapid liposomes: G. Toffano, A. Bruna, 829-845 (1980). Books: *Liposomes* of Gregoriadis, A. C. Allison, Eds. (Wiley), *Liposomes: From Physical Structureions*, C. G. Knight, Ed. (Elsevier, Am-348); *Liposome Technology*, G. GregoBoca Raton, 1984) 3 vols. nongenetic structures consisting of lipoens. Liposomes as immunological ad. G. Gregoriadis, *Nature* **252**, 252 (1974). enza virus vaccine: L. Thibodeau *et al.* it. Armand Frappier); rabies vaccine: P. **135E**, 183 (1984); vaccine against polyid bacteria: H. Snippe *et al.*, **EP 97407** recht). Antibodies to hepatitis B surface. Neurath *et al.*, *J. Gen. Virol.* **65**, 1009

Hormone. [9035-55-6] Lipotropin; pine; lipid-mobilizing hormone; adipolytic hormone; lipotrophin; LPH. Hypoich stimulates the release of fatty acids **β -LPH** is a single chain polypeptide cond residues and has been proposed as the for β -MSH and β -endorphin, *q.v.*, see M. *Biochem.* **57**, 1111 (1979). γ -LPH conds and is identical to the sequence of the LPH. Both contain sequences common to elanotropin, *q.v.* Sequences differ slightly species. Isolin and proposed structure of Li, *Nature* **201**, 924 (1964); Y. Birk, *C. H.* **2**, 1048 (1964); C. H. Li *et al.*, *Nature* **208**, Li, *Arch. Biol. Med. Exp.* **5**, 55 (1968). retien *et al.*, *Int. J. Peptide Protein Res.* **4**, id characterization of porcine β -LPH: Gi. *an. J. Biochem.* **48**, 1017 (1970). Amino rscine γ -LPH: Graf *et al.*, *Acta Biochim.*

Biophys. **5**, 305 (1970). Isolin, characterization of bovine β -LPH: P. Lohmar, C. H. Li, *Biochem. Biophys. Res. Commun.* **77**, 1088 (1977); of rat β -LPH: M. Rubinstein *et al.*, *Proc. Nat. Acad. Sci. USA* **74**, 3052 (1977); of whale β -LPH: H. Kawauchi *et al.*, *Int. J. Peptide Protein Res.* **15**, 171 (1980); of turkey β -LPH: W. C. Chang *et al.*, *ibid.* **261**. Initial isoln, partial structure of human β -LPH: G. Cseh *et al.*, *FEBS Letters* **2**, 42 (1968); *idem*, *ibid.* **21**, 344 (1972). Isolin, characterization, amino acid sequence of human β -LPH: C. H. Li, D. Chung, *Int. J. Peptide Protein Res.* **17**, 131 (1981). Review: D. T. Krieger *et al.*, *Recent Progr. Horm. Res.* **36**, 277-344 (1980).

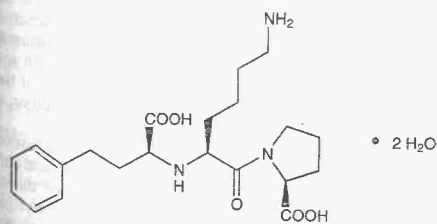
5537. Liranaftate. [88678-31-3] (6-Methoxy-2-pyridinyl)-methylcarbamothioic acid *O*-(5,6,7,8-tetrahydro-2-naphthalenyl) ester; *O*-5,6,7,8-tetrahydro-2-naphthyl *N*-(6-methoxy-2-pyridinyl)-*N*-methylthiocarbamate; pinitrate; M-732; Zefnart. $C_{20}H_{26}N_2O_2S$; mol wt 328.44. C 65.83%, H 6.14%, N 8.53%, O 9.74%, S 9.76%. Squalene epoxidase inhibitor. Prepn: **BE 897021**; T. Takematsu *et al.*, **US 4554012** (1983, 1985 both to Toyo Soda Manufacturing Co., Ltd.). Mode of action study: T. Morita *et al.*, *J. Med. Vet. Mycol.* **27**, 17 (1989). Antifungal spectrum: K. Iwata *et al.*, *Antimicrob. Ag. Chemother.* **33**, 2118 (1989). Physicochemical properties and stability: H. Awano *et al.*, *Iyakuhin Kenkyu* **23**, 558 (1992).



White crystalline powder, mp 98.5-99.5°. Soly (ml/g): acetone 10; chloroform 2; dehydrated ethanol 152; dichloromethane 2; ether 21; hexane 233; methanol 175; water >10000. Soly (mg/l): 0.10 (distilled water); 0.07 (buffer pH 1); 0.08 (buffer pH 4); 0.07 (buffer pH 7); 0.08 (buffer pH 11). Sol in benzene, dimethyl sulfoxide, *N,N*-dimethylformamide.

THERAP CAT: Antifungal.

5538. Lisinopril. [83915-83-7] (S)-1-[*N*-(1-Carboxy-3-phenylpropyl)-L-lysyl]-L-proline dihydrate; MK-521; Acerbon; Alapril; Carace; Coric; Novatec; Prinil; Prinivil; Tensopril; Vitec; Zestril. $C_{21}H_{31}N_3O_5 \cdot 2H_2O$; mol wt 441.52. C 57.13%, H 7.99%, N 9.52%, O 25.37%. Orally active angiotensin-converting enzyme (ACE) inhibitor. Prepn: A. A. Patchett *et al.*, **EP 12401**; E. E. Harris *et al.*, **US 4374829** (1980, 1983 both to Merck & Co.); M. T. Wu *et al.*, *J. Pharm. Sci.* **74**, 352 (1985). Comprehensive description: D. P. Ip *et al.*, *Anal. Profiles Drug Subs. Excip.* **21**, 233-276 (1992). HPLC determ in urine: Y. C. Wong, B. G. Charles, *J. Chromatog. B* **673**, 306 (1995). Series of articles in hypertension and congestive heart failure: *J. Med.* **85**, Suppl. 3B, 1-59 (1988). Review of clinical efficacy in myocardial infarction: K. L. Goa *et al.*, *Drugs* **52**, 564-588 (1996). Clinical trial in diabetic retinopathy: N. Chavvedi *et al.*, *Lancet* **351**, 28 (1998).



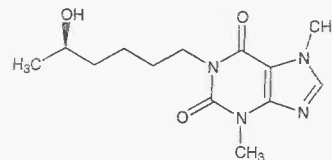
White to off-white crystalline, odorless powder. pK_{a1} (25°) 2.5; pK_{a2} 4.0; pK_{a3} 6.7; pK_{a4} 10.1. Approx uv max (0.1N NaOH): 246, 254, 258, 261, 267 nm ($A_{1cm}^{1\%}$ 4.0, 4.5, 5.1, 5.1, 5.7). (0.1N HCl): 246, 253, 258, 264, 267 nm ($A_{1cm}^{1\%}$ 3.2, 3.9, 4.5, 3.0, 2.8). $[\alpha]_{25}^{25} -120^\circ$ ($c = 1$ in 0.25M pH 6.4 zinc acetate); $[\alpha]_{25}^{25} -96^\circ$ ($c = 1$ in 0.25M pH 6.4 zinc acetate). Partition coefficient at room temp (0.1M pH 7 phosphate buffer/n-

octanol): 10.2 ± 0.5 . Soly (mg/ml): water 97; methanol 14; ethanol <0.1; acetone <0.1; acetonitrile <0.1; chloroform <0.1; DMF <0.1.

Mixture with hydrochlorothiazide. Prinzide.

THERAP CAT: Antihypertensive.

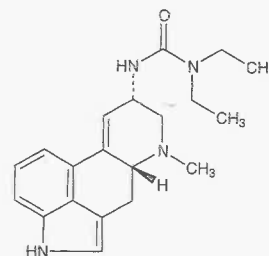
5539. Lisofylline. [100324-81-0] 3,7-Dihydro-1-[(5*R*)-5-hydroxyhexyl]-3,7-dimethyl-1*H*-purine-2,6-dione; 1-[(*R*)-5-hydroxyhexyl]theobromine; 1-(5*R*-hydroxyhexyl)-3,7-dimethylxanthine; CT-1501R; ProTec. $C_{13}H_{20}N_4O_3$; mol wt 280.32. C 55.70%, H 7.19%, N 19.99%, O 17.12%. Methylxanthine that inhibits production of phosphatidic acid during the inflammatory response. Identification as metabolite of pentoxifylline: H. J. Hinze *et al.*, *Arzneimittel-Forsch.* **22**, 1144 (1972). Enantioselective process: W. Aretz *et al.*, **DE 3942872**; *idem*, **US 5310666** (1991, 1994 both to Hoechst). Asymmetric synthesis: J. P. Klein *et al.*, **WO 95 31450** (1995 to Cell Therapeutics). Study of mechanism of action in septic shock: G. C. Rice *et al.*, *Proc. Nat. Acad. Sci. USA* **91**, 3857 (1994). Enhancement of hematopoietic recovery following 5-fluorouracil treatment in mice: E. Clarke *et al.*, *Cancer Res.* **56**, 105 (1996).



mp 110°. $[\alpha]_D^{20} -5.6^\circ$ ($c = 6.7$ in ethanol).

THERAP CAT: Immunomodulator.

5540. Lisuride. [18016-80-3] *N'*-[(8*α*)-9,10-didehydro-6-methylergolin-8-yl]-*N,N*-diethylurea; 9-(3,3-diethylureido)-4,6,6a,7,8,9-hexahydro-7-methylindolo[4,3-*f,g*]quinoline; 1,1-diethyl-3-(*D*-6-methylisoergolen-8-yl)urea; *N*-(*D*-6-methyl-8-isoergolenyl)-*N,N*-diethylurea; methylergol carbamide; lysuride. $C_{20}H_{26}N_4O$; mol wt 338.45. C 70.97%, H 7.74%, N 16.55%, O 4.73%. Dopamine D_2 -receptor agonist. Prepn: V. Zikan, M. Semonsky, *Coll. Czech. Chem. Commun.* **25**, 1922 (1960); *idem*, *Pharmazie* **23**, 147 (1968). Pharmacology and toxicity: Z. Votava, I. Lamplova, *Physiol. Bohemoslov.* **12**, 37 (1963). *C.A.* **59**, 9221d (1963).



Crystals from benzene, mp 186°. $[\alpha]_D^{20} +313^\circ$ ($c = 0.60$ in pyridine).

Maleate. [19875-60-6] Apodel; Cuvalit; Dopergin; Eunal; Lysenyl; Revanil. $C_{20}H_{26}N_4O \cdot C_4H_4O_4$; mol wt 454.52. Prisms from ethanol, mp 200° (dec). $[\alpha]_D^{20} +288^\circ$ ($c = 0.5$ in methanol). uv max (methanol): 313 nm. LD₅₀ i.v. in mice: 14.4 mg/kg (Votava, Lamplova).

THERAP CAT: Antimigraine; prolactin inhibitor; antiparkinsonian.

5541. Lita®. Protein-based fat mimetic consisting of water-dispersible microparticles of zein, *q.v.*, a hydrophobic prolamine derived from corn. Prepn: L. E. Stark, A. T. Gross, **US 5021248** (1991 to Enzytech); *idem*, **US 5145702** (1992 to Opta Food Ingrid.). Brief description: R. Iyengar, A. Gross in *Biotechnology and Food Ingredients*, I. Goldberg, R. Williams, Eds. (Van Nostrand Reinhold, New York, 1991) pp 287-313;