THE MERCK INDEX

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THIRTEENTH EDITION

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AN ENCYCLOPEDIA OF
CHEMICALS, DRUGS, AND BIOLOGICALS

THIRTEENTH EDITION

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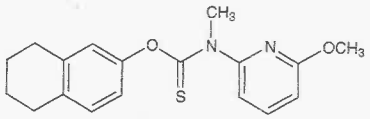
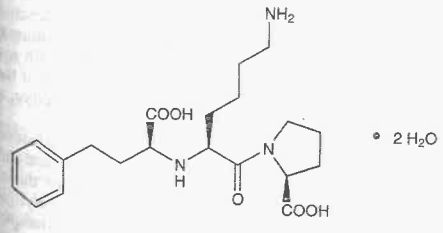
5537. Liranaftate. [88678-31-3] (6-Methoxy-2-pyridinyl)-methylcarbamothioic acid *O*-(5,6,7,8-tetrahydro-2-naphthalenyl) ester; *O*-5,6,7,8-tetrahydro-2-naphthyl *N*-(6-methoxy-2-pyridyl)-*N*-methylthiocarbamate; piritetrate; M-732; Zefnart. $C_{18}H_{20}N_2O_2S$; mol wt 328.44. C 65.83%, H 6.14%, N 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^2-(1-Carboxy-3-phenylpropyl)-L-lysyl]-L-proline dihydrate; MK-521; Acerbon; Alapril; Carace; Coric; Novatec; Prinil; Prinivil; Tensopril; Vivatec; Zestril. $C_{21}H_{31}N_3O_5.2H_2O$; 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 determn in urine: Y. C. Wong, B. G. Charles, *J. Chromatog. B* **673,** 306 (1995). Series of articles in hypertension and congestive heart failure: *Am. 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. Chavedi *et al., Lancet* **351,** 28 (1998).

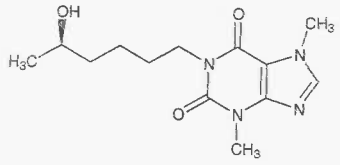


White to off-white crystalline, odorless powder. pKa_1 (25°) 2.5; pKa_2 4.0; pKa_3 6.7; pKa_4 10.1. Approx uv max (0.1*N* NaOH): 246, 254, 258, 261, 267 nm ($A^{1\%}_{1cm}$ 4.0, 4.5, 5.1, 5.1, 3.5, 3.0, 2.8). $[\alpha]^{25}_{405}$ −120° (c = 1 in 0.25*M* pH 6.4 zinc acetate); $[\alpha]^{25}_{436}$ −96° (c = 1 in 0.25*M* pH 6.4 zinc acetate). Partition coefficient at room temp (0.1*M* 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.

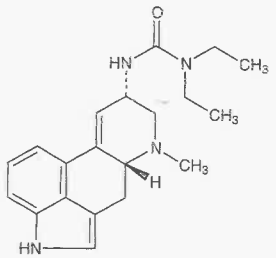
5539. Lisofylline. [100324-81-0] 3,7-Dihydro-1-[(5*R*)-5-hydroxyhexyl]-3,7-dimethyl-1*H*-purine-2,6-dione; 1-[(*R*)-5-hydroxyhexyl]theobromine; 1-(5*R*-hydroxyhexyl)-3,7-dimethylxanthine; CT-1501R; ProTec. $C_{13}H_{20}N_4O_3$; mol wt 280.32. C 55.70%, H 7.19%, N 19.99%, O 17.12%. Methylxanthine that 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**; *eidem,* **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°. $[\alpha]^{20}_{D}$ −5.6° (c = 6.7 in ethanol).

THERAP CAT: Immunomodulator.

5540. Lisuride. [18016-80-3] *N'*-[(8α)-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-*fg*]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); *eidem, 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°. $[\alpha]^{20}_{D}$ +313° (c = 0.60 in pyridine).

Maleate. [19875-60-6] Apodel; Cuvalit; Dopergin; Eunal; Lysenyl; Revanil. $C_{20}H_{26}N_4O.C_4H_4O_4$; mol wt 454.52. Prisms from ethanol, mp 200° (dec). $[\alpha]^{20}_{D}$ +288° (c = 0.5 in methanol). uv max (methanol): 313 nm. LD_{50} 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); *eidem,* **US 5145702** (1992 to Opta Food Ingred.). 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;