

Find authenticated court documents without watermarks at docketalarm.com.

## THE

# MERCK INDEX

AN ENCYCLOPEDIA OF CHEMICALS, DRUGS, AND BIOLOGICALS

#### THIRTEENTH EDITION

#### **Editorial Staff**

Maryadele J. O'Neil, Senior Editor Ann Smith, Senior Associate Editor Patricia E. Heckelman, Associate Editor

John R. Obenchain Jr., *Editorial Assistant* Jo Ann R. Gallipeau, *Technical Assistant* Mary Ann D'Arecca, *Administrative Associate* 

EDITION

DOCKE.

R

Μ

Δ

Susan Budavari, Editor Emeritus

Published by Merck Research Laboratories Division of

MERCK & CO., INC. Whitehouse Station, NJ

2001

Find authenticated court documents without watermarks at docketalarm.com.

### MERCK & CO., INC. Whitehouse Station, NJ USA

1st Edition-1889	
2nd Edition-1896	
3rd Edition-1907	
4th Edition-1930	
5th Edition-1940	
6th Edition-1952	
7th Edition-1960	
8th Edition-1968	
9th Edition-1976	
10th Edition-1983	
11th Edition-1989	
12th Edition-1996	
	_

Library of Congress Catalog Card Number 89-60001 ISBN Number 0911910-13-1

Copyright © 2001 by MERCK & CO., INC. All rights reserved. Copyright under the Universal Copyright Convention and the International Copyright Convention. Copyright reserved under the Pan-American Copyright Convention.

Printed in the USA

Find authenticated court documents without watermarks at <u>docketalarm.com</u>.

DOCKE

Δ

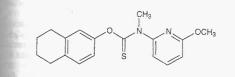
ap solutes and can interact with celcarry into cells biologically active ormally penetrate the plasma memosomes protects these materials from an cultures, from inactivation within atory system or, for pesticides and y rain or irrigation. Liposomes may le adsorption onto the cell surface, osome is delivered to the lysosoma! plasma membrane (liposome content plasm) and lipid exchange between without cell association of liposome used as models in biological memcental targeted drug delivery systems iologically active materials. See also and thermodynamics: J. N. Israe iophys. Acta 470, 185 (1977). Effec Toffano et al., "Phospholipid Lipe opamine Metabolism and on the Se ndocrinology: Biological and Clinical Macleod, Eds. (Academic Press, New Interaction with nucleic acids: B. Bro 'truct. Dyn. 1, 1535 (1984). Synthesis ologically active materials: D. P. P. toka, Jr., BE 874408 corresp to US for pesticides: eidem, US 4241046 ythrocytic malaria by liposomes con ds: C. R. Alving et al., Science 205. mology: H. E. Schaeffer, D. L. Krotn Sci. 22, 220 (1982). In delivery of spe tility control: L. Mettler, A. B. Czur to Nattermann). In transfer of nucle 2140822 (1984 to Stauffer). In get 1: C. Nicolau, Biochem. Soc. Trans. 12, phospholipid liposomes as drug deliv ascites tumor in mice: K. R. Patel of Acta 797, 20 (1984). Review of early al., ibid. 457, 259-302 (1976); of phar pid liposomes: G. Toffano, A. Brun 829-845 (1980). Books: Liposomes # Gregoriadis, A. C. Allison, Eds. (Wile) p; Liposomes: From Physical Structure tions, C. G. Knight, Ed. (Elsevier, Arr

-348; Liposome Technology, G. Grege Boca Raton, 1984) 3 vols. nunogenic structures consisting of lipe gens. Liposomes as immunological ad G. Gregoriadis, Nature 252, 252 (1974) enza virus vaccine: L. Thibodeau et al st. Armand Frappier); rabies vaccine P. . 135E, 183 (1984); vaccine against poly d bàcteria: 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 pinone; lipid-mobilizing hormone; adipolytic hormone; lipotrophin; LPH. Hype ich stimulates the release of fatty acids B-LPH is a single chain polypeptide concid residues and has been proposed as the for  $\beta$ -MSH and  $\beta$ -endorphin, q.v., see M. <sup>1</sup>. 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. Isoln and proposed structure of Li, Nature 201, 924 (1964); Y. Birk, C.H. ), 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 id characterization of porcine  $\beta$ -LPH: G an. J. Biochem. 48, 1017 (1970). Amin rcine v-LPH: Graf et al., Acta Biochine

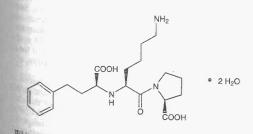
Biophys. 5, 305 (1970). Isoln, characterization of bovine B-LPH: P. Lohmar, C. H. Li, Biochem. Biophys. Res. Commun. 77, 1088 (1977); of rat β-LPH: M. Rubinstein et al., Proc. Nat. Acad. Sci. USA 74, 3052 (1977); of whale B-LPH: H. Kawauchi et al., Int. J. Peptide Protein Res. 15, 171 (1980); of turkey β-LPH: W. C. Chang et al., ibid. 261. Initial isoln, partial structure of human  $\beta$ -LPH: G. Cseh et al., FEBS Letters 2, 42 (1968); eidem, ibid. 21, 344(1972). Isoln, characterization, amino acid sequence of human B-LPH: C. H. Li, D. Chung, Int. 1. 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)nethylcarbamothioic acid O-(5,6,7,8-tetrahydro-2-naphthaenvl) ester; O-5,6,7,8-tetrahydro-2-naphthyl N-(6-methoxy-2yndyl)-N-methylthiocarbamate; piritetrate; M-732; Zefnart. H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>S; mol wt 328.44. C 65.83%, H 6.14%, N 8.53%. 09.74%, S 9.76%. Squalene epoxidase inhibitor. Prepn: BE \$97021; T. Takematsu et al., US 4554012 (1983, 1985 both to nyo Soda Manufacturing Co., Ltd.). Mode of action study: T. Morita et al., J. Med. Vet. Mycol. 27, 17 (1989). Antifungal ectrum: K. Iwata et al., Antimicrob. Ag. Chemother. 33, 2118 989). Physicochemical properties and stability: H. Awano et I. Iyakuhin Kenkyu 23, 558 (1992).



White crystalline powder, mp 98.5-99.5°. Soly (ml/g): acetone 10; chloroform 2; dehydrated ethanol 152; dichloromethand 2; ether 21; hexane 233; methanol 175; water >10000. Soly [1]: 0.10 (distilled water); 0.07 (buffer pH 1); 0.08 (buffer 14); 0.07 (buffer pH 7); 0.08 (buffer pH 11). Sol in benzene, menyl sulfoxide, N,N-dimethylformamide. THERAP CAT: Antifungal.

5538. Lisinopril. [83915-83-7] (S)-1-[N<sup>2</sup>-(1-Carboxy-3nylpropyl)-L-lysyl]-L-proline dihydrate; MK-521; Acerbon; april; Carace; Coric; Novatec; Prinil; Prinivil; Tensopril; Vi-Zestril. C<sub>21</sub>H<sub>31</sub>N<sub>3</sub>O<sub>5</sub>.2H<sub>2</sub>O; mol wt 441.52. C 57.13%, 799%, N 9.52%, O 25.37%. Orally active angiotensinaverting enzyme (ACE) inhibitor. Prepn: A. A. Patchett et . EP 12401; E. E. Harris et al., US 4374829 (1980, 1983 both Merck & Co.); M. T. Wu et al., J. Pharm. Sci. 74, 352 (1985). mprehensive description: D. P. Ip et al., Anal. Profiles Drug bt. Excip. 21, 233-276 (1992). HPLC determn in urine: Y. Wong, B. G. Charles, J. Chromatog. B 673, 306 (1995). mes of articles in hypertension and congestive heart failure: 1 J. Med. 85, Suppl. 3B, 1-59 (1988). Review of clinical Icacy in myocardial infarction: K. L. Goa et al., Drugs 52, 4-588 (1996). Clinical trial in diabetic retinopathy: N. Chavedi et al., Lancet 351, 28 (1998).



White to off-white crystalline, odorless powder.  $pKa_1$  (25°  $p_{ka_{2}}$  to ott-white crystalline, odoriess powder.  $p_{ka_{1}}$  (2.27)  $p_{ka_{2}}$  4.0;  $p_{ka_{3}}$  6.7;  $p_{ka_{4}}$  10.1. Approx uv max (0.1N OH): 246, 254, 258, 261, 267 nm ( $A_{1cm}^{1em}$  4.0, 4.5, 5.1, 5.1, 7): (0.1N HCI): 246, 253, 258, 264, 267 nm ( $A_{1cm}^{1em}$  3.2, 3.9), 3.0, 2.80,  $p_{12}$  (0.10) (0.10  $^{10}_{3,3,0,2,8}$  ( $\alpha$ )<sup>25</sup><sub>405</sub> -120° (c = 1 in 0.25*M* pH 6.4 zinc ace-traction ( $\alpha$ )<sup>25</sup><sub>405</sub> -120° (c = 1 in 0.25*M* pH 6.4 zinc ace- $\psi_{1,[\alpha]_{436}^{2,0}, [\alpha]_{405}^{2,0} = 120$  (c = 1 in 0.25*M* pH 6.4 zinc acetate). Parti-= coefficient at room temp (0.1*M* pH 7 phosphate buffer/*n*-

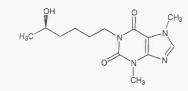
#### Lita®

octanol): 10.2  $\pm$ 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.

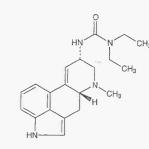
THERAP CAT: Antihypertensive.

5539. Lisofylline. [100324-81-0] 3,7-Dihydro-1-[(5R)-5hydroxyhexyl]-3,7-dimethyl-1H-purine-2,6-dione; 1-[(R)-5-hydroxyhexyl]theobromine; 1-(5R-hydroxyhexyl)-3,7-dimethylxanthine; CT-1501R; ProTec. C<sub>13</sub>H<sub>20</sub>N<sub>4</sub>O<sub>3</sub>; 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°.  $[\alpha]_{D}^{20} - 5.6^{\circ}$  (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-f,g]quinoline; 1,1diethyl-3-(D-6-methylisoergolen-8-yl)urea; N-(D-6-methyl-8-isoergolenyl)-N,N-diethylurea; methylergol carbamide; lysuride. C20H26N4O; mol wt 338.45. C 70.97%, H 7.74%, N 16.55%, O 4.73%. Dopamine D2-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°.  $[\alpha]_D^{20} + 313^\circ$  (c = 0.60 in pyridine).

Maleate. [19875-60-6] Apodel; Cuvalit; Dopergin; Eunal; Lysenyl; Revanil. C20H26N4O.C4H4O4; 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. LD<sub>50</sub> 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 5021240 (1002) to 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;

Find authenticated court documents without watermarks at docketalarm.com.