### Drug Metabolism Disposition:



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logical fate of chemicals

Editor RAYMOND F. NOVAK A publication of the American Society for Pharmacology and **Experimental Therapeutics** 

Founded in 1973 by Kenneth C. Leibman Vol. 24, No. 6 lune 1996



Published monthly by Williams & Wilkins

In this Issue:

Comparative Effects of Carbamazepine and Carbamazepine-10,11-epoxide on P450
Distribution of 1,2,3,4-Tetrahydro-9-acridinamine
Monohydrochloride Monohydrate and
Metabolites in Rat Brain
Metabolism in Mammalian Intestines and in Caco-2

Extrahepatic Metabolism of 4-Methylumbelliferone Human Microsomal Difluorovinyl Ether Metabolism Isolation and Bioactivity of Docetaxel Metabolites

Nonlinear Dorzolamide Pharmacokinetics in Rats Fatty Acid Epoxidation by P4502C2 and 2CAA Inactivation of P4502B1 by Deprenyl and Clorgyline Kinetics of Metabolism in Liver Slices and

Hepatocytes
Lipoic Acid Inhibits Glycine Conjugation
Mefloquine Enantiomers in Erythrocytes
Propranolol Oxidation by Recombinant CYP1A1 and

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Four copies of each manuscript should be sent to Dr. Raymond F. Novak, Editor, DRUG METABOLISM AND DISPOSITION, The Institute of Chemical Toxicology, Wayne State University, 2727 Second Avenue, Room 4000, Detroit, MI 48201-2654. Telephone: (313) 961-4943. Fax: (313) 961-0026 or 577-0082. Submission of a manuscript implies that the material contained therein has not previously been published except as an abstract for a scientific meeting, and that it is not being submitted elsewhere.

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  - 3. Abstract of not more than 250 words.
- 4. *Introduction*. A brief summary of the pertinent literature and a statement of the aims of the work.
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Equilibrium and kinetic constants:  $K_d$  (dissociation constant);  $K_s$  or  $K_i$  (dissociation constant of enzyme-substrate or enzyme-inhibitor complex);  $K_M$  (Michaelis constant);  $V_{\max}$  (maximum initial velocity); k (rate constant);  $pK_a$  (negative logarithm of acidic dissociation constant);  $t_{1/2}$ , half-life; AUC, area under the curve of plasma concentrations vs. time.

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Other abbreviations:  $^{\circ}$ C (degrees of temperature); g (acceleration due to gravity, as in 9000g); rpm (revolutions per min);  $LD_{50}$  and  $ED_{50}$  (median lethal and effective doses); iv (intravenous); ip (intraperitoneal); im (intramuscular); sc (subcutaneous); po (peroral); m.p. (melting point); sp.g. (specific gravity).

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**Frequency:** *Monthly*: One volume a year beginning in January. Printed on acid-free paper.

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### **Keynote Lecture**

Anthony Y. H. Lu (Merck; Rahway, NJ)

### **Pharmacogenetics and Cancer Chemotherapy**

Discussion Leader: William E. Evans (St. Jude's; Memphis, TN); Speakers: David Waxman (Boston U.; Boston, MA) "P450 activation of oxazaphosphorine anticancer drugs: development of a combined chemotherapy/gene therapy strategy." Frank Gonzalez (NCI; Bethesda, MD) "Genetic polymorphism of dihydropyrimidine dehydrogenase and 5-fluorouracil therapy: molecular mechanisms and clinical consequences." William Evans (St. Jude's; Memphis, TN) "Genetic polymorphism of thiopurine S-methyltransferase and thiopurine therapy: molecular mechanisms and clinical consequences."

### Pharmacogenetics of the Glutathione S-transferases

Discussion Leader: Peter van Bladeren (TNO/CIVO; The Netherlands); Speakers: Brian Ketterer (Univ. Coll.; London, England) "Class  $\theta$  glutathione S-transferases: mechanisms and relevance to variations in human risk." David Eaton (U. Wash.; Seattle, WA) "Class  $\alpha$  glutathione S-transferases: mechanisms and relevance to variations in human cancer risk."

### **Drug Metabolism in the Brain**

Discussion Leader: Henry Strobel (UT Med. School; Houston, TX); Speakers: Jean-Francois Ghersi-Egea (Institut Pasteur; Lille, France) "Roles of blood-brain barriers in cerebral drug metabolism." Hidenori Kawashima (UT Med. School; Houston, TX) "Brain cytochromes P-450 and mental diseases." Arthur Cooper (Cornell Univ.; NY) "Cysteine conjugate β-lyases."

### Drug Metabolism as a Determinant of Drug Toxicity

Discussion Leader: *David Jollow* (Med. Univ. S. Carolina; Charleston, SC); Speakers: *Arthur K. Cho* (UCLA; Los Angeles, CA) "The demethylation of methylenedioxyamphetamines by cytochromes P450." *Neal Castagnoli* (VPI and State U.; Blacksburg, VA) "Biotransformation of cyclic tertiary amines to neurotoxic metabolites."

### Phase III Metabolism: The Export of Drugs and Metabolites

Discussion Leader: Terrence J. Monks (U. Texas; Austin, TX); Speakers: Piet Borst (Nederlands Kanker Inst. Amsterdam; The Netherlands) "The GS-X pump." Jeff Silverman (NCI; Bethesda, MD) "Xenobiotic regulation of the rat multi-drug resistance lb gene." Mary Vore (U. Kentucky; Lexington, KY) "Does canalicular P-glycoprotein mediate estrogen glucuronide cholestasis?"

### **Drug Metabolism Data Blitz**

Discussion Leader: Serrine S. Lau (U. Texas; Austin, TX); Selected presentations from conferees.

### Drug Metabolism in Drug Discovery and Drug Development

Discussion Leader: Brian Smith (SmithKline Beecham; King of Prussia, PA); Speakers: Brian Smith (SmithKline Beecham; King of Prussia, PA) "Strategies to facilitate the discovery to development transition." Andrew Ayrton (SmithKline Beecham; King of Prussia, PA) "In vitro biotransformation in the drug discovery process." Martin Dyroff (Zeneca; Wilmington, DE) "The role of drug metabolism and pharmacokinetics during drug hunting and optimization."

### **Technological Advances in Drug Metabolism**

Discussion Leader: Ronald E. White (Bristol Myers-Squibb; Princeton, NJ); Speakers: Jeremy K. Nicholson (Univ. London; England) "HPLC-NMR studies on drug metabolism, and drug metabolite reactivity." Daniel E. Murnick (Rutgers Univ.; Newark, NJ) "Laser-assisted isotope ratio analysis of C, N, and O."