Drug Metabolism and Disposition:
the biological fate of chemicals

May/June 1994

CONTENTS

LETTER TO THE EDITOR

Are Routine Tissue Distribution Studies Justifiable for Approval of Human Drugs? A. M. MONRO 341

ARTICLES

Inactivation of Purified Rat Liver Cytochrome P-450 2B1 and Rabbit Liver Cytochrome P-450 2B4 by N-Methylcarbazole. STEVEN C. KUEMMERLE, TING-LIANG SHEN, AND PAUL F. HOLLENBERG 343

In Vitro Metabolism of Zatosetron: Interspecies Comparison and Role of CYP 3A. BARBARA J. RING, C. JOHN PARLI, MALCOLM C. GEORGE, AND STEVEN A. WRIGHTON 352

Pharmacokinetics and Kinetic-Dynamic Modeling of an 8-Aminoquinoline Candidate Anticyanide and Antimalarial Drug (WR242511). MARK T. MARINO, JAMES O. PEGGINS, LARRY D. BROWN, MICHAEL R. URQUHART, AND THOMAS G. BREWER 358

Carbonyl Reductase Activity for Acetohexamide in Human Erythrocytes. M. KISHIMOTO, R. KAWAMORI, T. KAMADA, AND T. INABA 367

Cloning, Expression, and Functional Characterization of Two Mutant (NAT2*) and Wild-Type Human Polymorphic N-Acetyltransferase (NAT2) Alleles. RONALD J. FERGUSON, MARK A. DOLL, TIMOTHY D. RUSTAN, KEVIN GRAY, AND DAVID W. HEIN 371

Binding of Dorzolamide and Its Metabolite, N-Deethylated Dorzolamide, to Human Erythrocytes in Vitro. TAKURO HASEGAWA, KEN’ICHI HARA, AND SHUNSUKE HATA 377

Indole-3-carbinol and β-Naphthoflavone Induction of Aflatoxin B1 Metabolism and Cytochromes P-450 Associated with Bioactivation and Detoxication of Aflatoxin B1 in the Rat. D. M. STRESSER, G. S. BAILEY, AND D. E. WILLIAMS 383

Indole-3-carbinol Induces a Rat Liver Glutathione Transferase Subunit (Yc2) with High Activity toward Aflatoxin B1, exo-Epoxide: Association with Reduced Levels of Hepatic Aflatoxin-DNA Adducts in Vivo. D. M. STRESSER, D. E. WILLIAMS, L. I. MCLELLAN, T. M. HARRIS, AND G. S. BAILEY 392

Nonlinear Kinetics of Alendronate: Plasma Protein Binding and Bone Uptake. JIUN H. LIN, I-WU CHEN, AND FLORENCIA A. DELUNA 400

Disposition Kinetics of d- and l-Amphetamine following Intravenous Administration of Racemic Amphetamine to Rats. ATHIWAYAT HUTCHALEEJAH, JUTHAMAS SUKBUNTHERING, HSIAO-HUI CHOW, AND MALCOLM MAHERSON 406

Hepatic Microsomal Azoreductase Activity: Reactivity of Azo Dye Substrates Is Determined by Their Electron Densities and Redox Potentials. SHMUEL ZBaida, C. FRED BREWER, AND WALTER G. LEVINE 412

Reversible and Irreversible Interactions of a Cisplatin Analog Bearing a 1,2-Diphenylethylenediamine Ligand with Plasma and Plasma Proteins in Vitro. PATRICK J. BEDNARSKI, NICOLE A. KRATOCHWILL, AND ANGELA M. OTTO 419


Metabolism of Thapsigargin in Rat Hepatocytes. MALENE S. NIELSEN, CARL E. OLSEN, JOHN DICH, BRÖGGER CHRISTENSEN, AND NIELS GRUNNET 433

Urinary and Biliary Disposition of the Lactone and Carboxylate Forms of 20(S)-Camptothecin in Rats. DENNIS O. SCOTT, DILBIR S. BINDRA, STEVEN C. SUTTON, AND VALENTINO C. CARBOCCHI 438

Brain Uptake and Biotransformation of Remacemide Hydrochloride, a Novel Anticonvulsant. HELEN HEYN, DENNIS J. MCCARTHY, STEPHEN H. CURRY, MARK S. EISMAN, AND M. W. ANDERS 443

Continued on next page
ANNOUNCEMENT

Effective January 1, 1994 all manuscripts for submission to DRUG METABOLISM AND DISPOSITION: THE BIOLOGICAL FATE OF CHEMICALS should be sent to:

Raymond F. Novak, Editor
Institute of Chemical Toxicology
Wayne State University
2727 Second Avenue, Room 4000
Detroit, Michigan 48201-2654

Telephone 313–961–4943
Fax 313–577–0082

<table>
<thead>
<tr>
<th>Study Title</th>
<th>Authors</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Studies on the Renal Excretion Mechanisms of Cefadroxil</td>
<td>Luis Granero, Maria Jose Gimeno, Francisca Torres-Molina, Jesus Chesa-Jimenez, Jose Esteban Peris</td>
<td>447</td>
</tr>
<tr>
<td>A New Analysis Method for Disposition Kinetics of Enterohepatic Circulation of Diclofenac in Rats.</td>
<td>Takako Fukuyama, Kiyoshi Yamaoka, Yuka Ohata, and Terumichi Nakagawa</td>
<td>479</td>
</tr>
<tr>
<td>N-Hydroxylation of the Antiprotozoal Drug Pentamidine Catalyzed by Rabbit Liver Cytochrome P-450 2C3 or Human Liver Microsomes, Microsomal Retroreduction, and Further Oxidative Transformation of the Formed Amidoximes: Possible Relationship to the Biological Oxidation of Arginine to N⁶-Hydroxyarginine, Citrulline, and Nitric Oxide.</td>
<td>James A. Vitarius and Lester G. Sultatos</td>
<td>486</td>
</tr>
<tr>
<td>SHORT COMMUNICATION</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cocaine Pharmacokinetics in Ethanol-Pretreated Rats.</td>
<td>Barry S. Levine and Ian R. Tebbett</td>
<td>498</td>
</tr>
<tr>
<td>Erratum</td>
<td></td>
<td>501</td>
</tr>
</tbody>
</table>