Comparison of Plasma Creatinine Levels in Patients Determined by High-Pressure Liquid Chromatography, Automated Analysis, and Boiling Alkaline Picrate Method

Keyphrases □ Creatinine—analyses by high-pressure liquid chromatography, automated analysis, and alkaline picrate method compared, human plasma □ High-pressure liquid chromatography—analysis, creatinine in human plasma, compared to automated analysis and alkaline picrate method □ Automated analysis—creatinine in human plasma, compared to high-pressure liquid chromatography and alkaline picrate method □ Alkaline picrate—analysis, creatinine in human plasma, compared to high-pressure liquid chromatography and automated analysis method

To the Editor:

Accurate determinations of endogenous creatinine levels in plasma or serum are important to the diagnosis of renal function and the modification of dosage regimens in patients with renal diseases (1, 2). The potential interference problems associated with many presently used procedures have been reviewed (3, 4).

This communication reports findings on the plasma creatinine levels as determined by three different methods using the same batch of plasma samples from some 30 patients with various degrees of renal function. These creatinine assays included an automated analysis[1] routinely performed in many hospitals, a boiling alkaline picrate method (5), and a rapid, micro high-pressure liquid chromatographic (HPLC) method recently developed in this laboratory (4).

The HPLC method involves vortex mixing of plasma with acetonitrile (1:2.5 v/v) and chromatographing the supernate on an ion-exchange column, using acidified 0.1 *M* ammonium phosphate as the mobile phase. Although ammonium chloride was used in earlier studies, ammonium phosphate offers the same separation and is superior in inertness toward the HPLC system.

The results are summarized in Table I. In general, the values obtained from the boiling alkaline picrate method were higher than those from automated analysis which, in turn, were greater than those from HPLC. The average creatinine levels of these plasma samples assayed by the automated analysis and the boiling alkaline picrate method were 14.55% (n = 30) and 32.41% (n = 28), respectively, greater than the level obtained by HPLC. The differences ranged from −12.8 to +45.2% for the automated analysis and from −15.3 to +101.6% for the boiling alkaline picrate method.

Table I—Comparison of Plasma Creatinine Levels of Patients Determined by Three Different Methods

	Creatinine Levels, mg % Determined by			Percent Deviation from HPLC	
Patient	HPLC	Automated Analysis	Boiling Alkaline Picrate	Automated Analysis	Boiling Alkaline Picrate
1	2.16	2.2	2.63	+1.85	+21.76
2	2.62	3.2	3.70	+22.14	+41.22
3	2.79	3.8	3.90	+36.20	+39.78
4	5.79	7.4	7.43	+27.81	+28.32
5	1.63	2.2	2.43	+34.97	+49.08
6	2.42	3.3	4.10	+36.36	+69.42
7	2.21	2.7	2.82	+2.17	+27.60
8	0.65	0.7	1.25	+7.69	+92.31
9	0.68	0.8	1.16	+17.65	+70.59
10	0.62	0.9	1.25	+45.16	+101.61
11	0.91	1.0	1.45	+9.89	+59.34
12	1.88	2.2	2.53	+17.02	+34.57
13	1.90	2.3	3.02	+21.05	+58.95
14	2.10	2.6	3.12	+23.81	+48.57
15	2.92	3.2	3.61	+9.59	+23.63
16	3.00	3.3	3.51	+10.00	+17.00
17	4.08	4.1	4.29	+0.49	+5.15
18	4.35	4.4	4.98	+1.15	+14.48
19	4.95	4.6	5.47	−7.07	+10.51
20	4.29	4.6	5.27	+7.23	+22.84
21	6.08	5.3	5.67	−12.83	−6.74
22	5.35	5.8	5.96	+8.41	+11.40
23	8.46	8.7	8.70	+2.84	+2.84
24	9.50	10.2	9.29	+7.37	−2.21
25	13.33	12.9	11.35	−3.22	−14.85
26	12.92	14.1	13.51	+9.13	+4.57
27	18.50	18.6	15.67	+0.54	−15.30
28	10.67	12.3	12.24	+15.28	+12.83
29	9.67	10.2	—	+5.48	—
30	15.00	16.8	—	+12.00	—
				Mean ± SD 14.55 ± 11.87	32.41 ± 27.26

The overestimation of plasma or serum creatinine levels determined by either the automated analysis or manual method using the principle of complexation between creatinine and picric acid is well documented (4). This overestimation is due to the presence of endogenous substances (pseudocreatinine), which also can react with the picrate reagent. The results of the present study are consistent with these previous findings, since the HPLC method is

[1] SAM-6, Technicon Instruments Corp., Tarrytown, N.Y.

free of these interferences and only measures the "true" creatinine.

The boiling alkaline picrate method has been claimed to measure the true creatinine (5). The results of the present study do not support the claim. In a previous study (3), the "apparent" recovery of the spiked creatinine in plasma was only 81% and, after heat treatment, certain components in plasma were thought to suppress the creatinine–picrate complex reaction or to interfere with the color formation. Thus, the reason for the higher creatinine values by the boiling alkaline picrate method remains to be determined.

(1) W. L. Chiou and F. H. Hsu, *J. Clin. Pharmacol.*, **15**, 427 (1975).
(2) W. L. Chiou and F. H. Hsu, *Res. Commun. Chem. Pathol. Pharmacol.*, **9**, 315 (1975).
(3) W. L. Chiou, F. H. Hsu, and G. W. Peng, *Clin. Chem.*, **23**, 1374 (1977).
(4) W. L. Chiou, M. A. F. Gadalla, and G. W. Peng, *J. Pharm. Sci.*, **67**, 182 (1978).
(5) H. Yatzids, *Clin. Chem.*, **21**, 1848 (1975).

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BOOKS

REVIEWS

Practical Clinical Pharmacy. Edited by CHARLES A. WALKER and JOHN R. FOXX. Stratton, 381 Park Avenue South, New York, NY 10016. 1977. x + 142 pp. 15 × 23 cm. Price $16.95.

The reader approaches a book called "Practical Clinical Pharmacy" with expectations of gaining insight into techniques of monitoring drug therapy, strategies for improving pharmacist–prescriber and pharmacist–patient communications, and data on the clinical pharmacology and therapeutic use of drugs. What the reader receives in lieu of this critical information is a collection of philosophical discussions on the role and potential for clinical pharmacy practice.

The book contains 14 presentations delivered at the "First Annual Symposium on a Clinical Pharmacy Program" sponsored by the School of Pharmacy at Florida A & M University; the date of the symposium is not disclosed. The presentations are organized under three themes: (*a*) the clinical curricula, (*b*) the role and liabilities of a clinical pharmacist, and (*c*) other health professionals' view of clinical pharmacy. The most informative discussions are by Roger Palmer on "The Role of Clinical Pharmacology and Pharmacokinetics in a Clinical Pharmacy Program" and by Charles Walker and Karam Soliman on "The Clinical Pharmacist's Role in Research and Therapeutics."

Perhaps the book is an appropriate addition to health professions libraries. It is an unlikely choice for personal purchase.

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Design of Biopharmaceutical Properties through Prodrugs and Analogs. Edited by EDWARD B. ROCHE. American Pharmaceutical Association, 2215 Constitution Avenue, N.W., Washington, DC 20037. 1977. 455 pp. 16 × 23 cm. Price $20.00, $13.00 Member Rate.

This series of 15 papers was presented at Orlando in November 1976 and published less than 1 year later! Congratulations to the editor, authors, and APhA.

Papers of particular interest are "Structural Aspects of Selective Distribution" by Roche with 34 references, which provides a good background for "Structural Effects of Partitioning Behavior of Drugs" by Dunn (13 references), and "Correlation Analysis in the Design of Pharmacodynamic Properties of Drugs" by Hansch (12 references). Also of special interest are "Alteration of Pharmacokinetics through Structural Modification" by Notari (34 references), "Novel Approaches for the Design of Membrane Transport Properties of Drugs" by Bodor (38 references), and "Physical Model Approach to the Design of Drugs with Improved Intestinal Absorption" by Ho, Park, Morozowich, and W. Higuchi. The latter, with 91 pages (89 references), is well worth the price of the book. It should be of particular value to students.

"The Prediction of Chemical Liability through Substituent Effects" by Charton (68 references) contains a wealth of tabulated data and constants. In "Alteration of Drug Metabolism through Structural Modification" by Nelson is a very useful list of 112 pertinent references. Finally, Morozowich, Cho, and Kezdy put it all together in "Application of Physical Organic Principles to Prodrug Design" (93 references).

Considering the applied nature of this approach to designing useful agents, the editor might have given greater emphasis to the practical consideration that such modifications result in new compounds in the sense of requiring extensive and costly safety studies and provide no short cut in this critical area of testing. Also, it would have been helpful for those interested in this general approach to have at least listed the related approaches of molecular complexes, alternate salts, solid solutions, liposomal transport, *etc.*, as means of achieving useful drug modification.

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Aspirin and Related Drugs: Their Actions and Uses. Edited by K. D. RAINSFORD, K. BRUNE, and M. W. WHITEHOUSE. Birkhauser Verlag, P. O. Box 34, CH-4010 Basel, Switzerland. 1977. 118 pp. 17 × 24 cm.

The 11 papers and introductory comments contained in this volume comprise the Symposium on Aspirin and Related Drugs held in conjunction with the Physiology Section, 47th Congress of the Australian and New Zealand Association for the Advancement of Science, on May 14, 1976 at the University of Tasmania, Hobart, Australia. The compilation of these papers provides a useful overview of the current research trends in Australia in the areas of salicylate pharmacology and toxicology.

While this book is not a comprehensive review of the pharmacology of nonsteroidal anti-inflammatory agents, it does provide insight into some current theories of anti-inflammatory and gastrotoxic mechanisms of action. Theories of anti-inflammatory modes of action discussed in this book include both the inhibition and stimulation of microsomal