



Figure 2—A comparison of Δ_X and π_X (heptane-water) values for common substituents with benzene as the reference standard. Key: (—) π_X (heptane-water) = Δ_X .

heptane, as evidenced by small water content of $3.3 \times 10^{-3} M$ at saturation (10), makes it sensitive to the difference in polarity between a substituted and parent (benzene) molecules. With $X = \text{NH}_2, \text{CHO}, \text{NO}_2, \text{CN}, \text{COCH}_3, \text{COOH}$, and CH_2COOH attached to benzene, the observed π_X (heptane-water) values are markedly lower than the corresponding Δ_X values. These results presumably from greatly increased polarities of the substituted benzenes (over that of benzene), which reduce the compatibilities of the substituted benzenes with heptane. Addition of alkyl groups to benzene (making the molecules more hydrocarbon-like) gives somewhat higher π_X (heptane-water) than π_X (octanol-water), as would be expected. Addition of halogen groups shows insignificant differences between the two sets of π_X values. In other words, the values of $\log[(\gamma_0^*)_X/(\gamma_0^*)_R]$ in the heptane phase are reasonably close to zero for relatively nonpolar substituents but are very significant and positive for polar substituents. As a whole, those substituents which cause large differences between π_X (heptane-water) and Δ_X are the same ones that show large differences between π_X (heptane-water) and π_X (octanol-water).

In conclusion, the correspondence between Δ_X and π_X in heptane-water is less obvious than in octanol-water, because heptane shows greater sensitivity than octanol to the polarities of the substituted benzenes.

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Received December 24, 1981.

Accepted for publication July 30, 1982.

Supported by U.S. Public Health Grants ES-02400 and ES-00210 and by U.S. Environmental Protection Agency Cooperative Research Fund CR-808046 from the EPA Environmental Research Laboratory at Corvallis, Ore.

Effect of Water Deprivation on Chloramphenicol Disposition Kinetics in Humans

Keyphrases □ Kinetics, disposition—effect of water deprivation on chloramphenicol, humans □ Chloramphenicol—effect of water deprivation, disposition kinetics in humans

To the Editor:

The first study of the effect of water deprivation on drug disposition kinetics was recently reported (1). Temporary water deprivation causes significant changes in drug metabolizing enzymes, hormones responsible for water balance in the body, and blood chemistry and physiology (2–4). Despite these significant changes, little has been reported in the literature on the effect of water deprivation resulting from various disease states and environmental factors on drug disposition kinetics.

The present study reports the effect of highly restricted water intake on chloramphenicol absorption and urinary elimination in humans.

The panel of subjects studied consisted of four healthy male volunteers (weight, 60–72 kg; age, 22–24 years). A total of 14 days was allowed for the conditioning of the subjects for the treatment studies. During the first 11 days,

each was allowed 1 liter of water/day, for the next 2 days only 350 ml/day, and 24 hr before the study only 200 ml of water/day. All subjects were fasted overnight. The treatment studies began at 8 am when chloramphenicol was given as 10 ml of suspension¹ (250 mg) with 150 ml of water. Urine samples were collected afterward on a periodic basis during an interval of 24 hr and analyzed for chloramphenicol using a previously described method (5). A 2-week wash-out period was allowed between control and treatment studies. In the control studies, which preceded the treatment studies, food and water were available *ad libitum*. Otherwise, conditions of the control studies were the same as for the treatment studies. The data of Table I show the effect of water deprivation on the absorption rate and the urinary excretion of chloramphenicol. Although there was no significant change in the total absorption of chloramphenicol, the absorption half-life decreased significantly (~66%), while the peak excretion rate increased, and the time at which the peak excretion occurred decreased significantly.

These findings are of great interest, since the overall effect of water deprivation is specified in terms of the rate of absorption change, which results in the substantially higher plasma levels of chloramphenicol in the water deprivation state. The influence of such (water deprivation) alteration in the peak plasma levels of chloramphenicol on

Table I—Urinary Excretion Characteristics of Chloramphenicol in Water Deprivation

	Control ^a	Water Deprivation ^a
Percent recovery	91 ± 12	103 ± 3
Peak excretion rate, mg/hr	23.06 ± 4.74	35.71 ± 4.92
Peak concentration time, hr	4.5 ± 0.3	2.5 ± 0.3
<i>t</i> _{1/2} absorption, hr	1.8 ± 0.3	0.6 ± 0.1

^a Mean ± SD; all values statistically different at *p* < 0.05 except those pertaining to the percent recovery, which were not significantly different.

the efficacy and toxicity of this antibiotic will profoundly affect its clinical utility. These observations are the first of their kind, and mechanisms for the effects observed remain to be investigated.

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Received March 3, 1982.

Accepted for publication August 4, 1982.

¹ Chloromycetin palmitate suspension, Parke-Davis Co., Karachi, Pakistan.

BOOKS

REVIEWS

ISI Atlas of Science. By Dr. EUGENE GARFIELD. Institute of Scientific Information, 3501 Market Street, University City Science Center, Philadelphia, PA 19104. 1982. 540 pp. 23 × 29 cm. Price \$45.00 to individuals, \$90.00 to institutions.

The *ISI Atlas of Science* is a new information and research guide in biochemistry and molecular biology. The *Atlas* is a unique new aid containing concise, convenient lists of papers and current literature in 102 active research areas in the life sciences.

This atlas contains a reference system of core clusters of research areas identified objectively by the use of citation patterns of publishing scientists, graphically displayed in detail by the use of maps.

Research areas described in the *Atlas* are divided into minireviews, core document bibliographies, specialty maps, and key citing document bibliographies. Also included within this atlas is a unique multi-colored fold-out map providing a "global" view of the relationships and interactions of the 102 research areas, ideal for display in labs, classrooms, and libraries.

The *Atlas* was designed to be used as a tool for analytical and utilitarian research needs. This publication should be a valuable tool for specialists in biochemistry and molecular biology for overviews of new fields of research and fields related to present work. Librarians can use the *Atlas* for subject bibliographies. This should also be of interest to historians for bibliographic and analytical information in tracing the structure and growth of scientific fields.

Staff Review

Drug Absorption. Edited by L. F. PRESCOTT and W. S. NIMMO. Adis Press, 404 Sydney Road, Balgowlah, NSW 2093, Australia. 1979. 353 pp. 16 × 24 cm.

This multi-authored book describes the proceedings of an international conference of Drug Absorption which was held in Edinburgh in September 1979.

The editors of the book are recognized authorities in the field of drug absorption, and the many authors who have contributed to the 31 chapters represent a broad, international array of specialists in this area.

Topics covered include anatomical and physiological factors affecting absorption, membrane effects, rectal absorption, presystemic and intestinal metabolism, toxicity, formulations and novel drug delivery systems, transdermal and controlled GI drug absorption, effect of age and disease states on drug bioavailability, methods of assessing drug absorption, *in vitro-in vivo* correlations, and problems in the assessment of drug absorption. The concluding chapter summarizes the viewpoints of regulatory agencies, clinical pharmacology, and of the pharmaceutical industry on drug bioavailability and pharmacokinetic studies.

Most of the chapters contain a discussion section, and all chapters are adequately referenced. A subject index is included.

This is a useful and instructive book that is broad-reaching in scope. The extensive coverage of many factors related to drug absorption, and the clear and articulate way in which the material is presented, makes it a required text for those interested in this broad area of research and clinical practice.

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