Book Reviews

USAN 10 and the USP Dictionary of Drug Names. Published by the United States Pharmacopeial Convention, Inc., and printed by Mack Printing Company, Easton, Pa. 1972. xii + 184 pp. 21 × 28 cm. $15.00.

Since 1961, an annual, cumulative compilation of United States Adopted Names (usually abbreviated, USAN) and other names for drugs have been published under the auspices of the United States Pharmacopeial Convention which is one of the three organizations which sponsor the USAN program and form the USAN Council. (The other two sponsors are the American Medical Association and the American Pharmaceutical Association and, since 1967, a liason representative from the Food and Drug Administration also sits on the USAN Council.) The USAN program has as its purpose the assignation of nonproprietary drug names as they are developed with such names intended to be "useful primarily to health practitioners, especially physicians, dentists, veterinarians, pharmacists, and nurses." The USAN Council members select the nonproprietary name according to their published principles, "the primary purpose of which is to assure consistency in the choice of names of maximal usefulness."

This current volume is the tenth compilation of United States Adopted Names being cumulative for such names from June 15, 1961 through 1971. The format and the outlook of the publication has been changed, however, from preceding volumes. The book is now about 70% larger in page size than formerly and has a two-column arrangement of entries. The entries have been enlarged to 5055 in number and changed in organizational arrangement to present a single, consolidated, alphabetic list of the following: (1) United States Adopted Names (1142 of the total entries); (2) official names of drug substances from the current edition of the United States Pharmacopeia and National Formulary; (3) older names in general use prior to 1961; (4) official names established by the FDA; (5) brand names; and (6) code designations used by various investigators or manufacturers of drug substances. These changes represent an attempt to not only disseminate the U. S. Adopted Names as widely as possible but to serve as a dictionary of names of all kinds of drugs whether public, private, chemical, or code-designated names.

The amount of information provided with each entry varies in scope with USAN entries the most complete. For USAN entries the following is included: U. S. Adopted Name; year of publication as a USAN; pronunciation guide; molecular and graphic formula; systematic chemical name; *Chemical Abstract Service* register number; pharmacologic activity claim; brand name(s) currently or formerly in use; name(s) of manufacturer(s) or distributor(s); code designation(s). For current USP and NF entries far less information is given since it is believed that reference to these sources can provide any more information desired.

In addition to the largest section devoted to alphabetic listing of drug names, other sections or appendixes give a listing of CAS registry numbers of drugs included in the volume; USAN and current USP and NF names listed in categories according to their usage or activity; guiding principles for coining U. S. Adopted Names for drugs; molecular formulas and corresponding USAN; names and addresses of domestic firms associated with compounds for which USAN have been chosen.

This book is improved in usefulness over previous volumes by its enlarged list of entries and new consolidated, alphabetic listing arrangement. It probably should be part of any library servicing persons interested in drugs whether such persons are actual professional practitioners in the various health sciences or researchers in the basic sciences associated with drugs. It is not likely that individuals would find it so frequently useful to warrant acquisition of personal copies particularly since annual, cumulative volumes apparently will continue to appear.

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Advanced Immunochemistry. By Eugene D. Day. Williams and Wilkins, Baltimore, Md. 1972. xvi + 447 pp. $19.00.

This precise, well-written, but certainly nonelementary, immunochemical text is divided into two approximately equal parts. The first part, appearing at a most propitious moment in view of the recent Nobel award to Edelman and Porter for their investigations into the structure of antibodies, is concerned with just that subject. Consisting of four chapters, it provides detailed reviews of (a) the light and heavy chains of immunoglobulins with emphasis on sequential analyses and genetic variabilities, (b) the sizes and shapes of different classes of antibodies, and (c) the combining sites of antibodies. The second part of the book is concerned with the reactions of antibodies. Various equations and physicochemical parameters are defined and derived and the thermodynamic treatment extends to the reactions of antibodies with haptens as well as with multivalent antigens. There is also a chapter on the active centers of multivalent antigens which includes an excellent discussion of both conformational and sequential dependencies of antigenic determinants.

The book is up to date and includes literature references through 1970. Tables and figures are both plentiful although the latter are generally of various plots and curves obtained directly from the literature rather than of the schematic type that are designed to further an understanding of a difficult or complicated point.

Clearly, any scientist with immunochemical training, knowledge, or experience will find this a useful book. It is written with just the right amount of historical perspective and the chapter describing the antibody-combining site will prove of particular interest to any medicinal scientist familiar with the analogous problems posed by agonist- and antagonist-receptor interactions.

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Folate Antagonists as Chemotherapeutic Agents. Annals of the New York Academy of Sciences. Vol. 186. Edited by Joseph R. Bertino with 90 contributors. N. Y. Academy of Sciences, New York, N. Y. 1971. 519 pp. 15 × 22.7 cm. Paperback. $27.00.

This monograph is a compilation of papers presented at a conference on folate antagonists convened by the N. Y. Academy of Sciences in Jan 1971. The format follows closely that of the conference, and the book is divided into six parts covering the principal areas of folate antagonists research under the following headings: folate compounds–chemistry and enzymology, dihydrofolate reductase, design and synthesis of folate antagoninsts, cytotoxic mechanisms of folate antagonists, pharmacologic considerations, and present status and future prospects for chemotherapy with folate antagonists. Certain aspects of folate biochemistry that deserve further investigation have been delineated. Recent advances in pmr studies of folate and antagonists reported at the conference promise to facilitate greatly the characterization of these compounds.

As an ever-increasing variety of well-described dihydrofolate reductase (DHFR) from diverse sources has been discovered in recent years, it is gratifying for Huennekens, *et al.*, to caution against the careless extrapolation of properties from one DHFR to another. Nonetheless, DHFR's from mammalian cells seem to bear more resemblance among themselves than to enzymes from other sources. Kinetic studies by Blakley, *et al.*, with two DHFR sensitive and resistive to methotrexate (amethopterin, MTX), isolated from *Streptococcus faecium*, have shown that considerable differences exist in the stereochemistry of the active site, notwithstanding the similarity in kinetic constants. It would be relevant to perform analogous investigations with mammalian cells, especially human tumor cells responsive and refractory to MTX. A well-recognized cellular event modified by MTX involves its inhibition of DHFR; however, other effects of MTX should not be lightly overlooked, for example, the induction of thymidylate synthetase in partially hepatomized rats. Future experiments to elucidate other possible mechanisms of action of folate antagonists are clearly indicated.

Since the introduction of MTX into clinical medicine more than a quarter of a century ago, hundreds of folate antagonists have been synthesized; yet MTX remains today the only folate antagonist of practival importance for the treatment of neoplastic diseases, leukemia in particular. Despite this hegemony, MTX, in common with most cancer chemotherapeutic agents, suffers from a number of drawbacks thus far insurmountable. Among the more serious ones are: the lack of selective cytotoxicity to cancer cells, the failure to reach the "sanctuary" of sequestered tumor cells, and the tendency to induce cellular resistance. For years these problems have been taxing

the ingenuity and resourcefulness of medicinal chemists; a few of the leading ones have now contributed to the present volume. The late B. R. Baker, undoubtedly one of the most imaginative and productive contemporary medicinal chemists, presented a lucid account of his systemic search for "active-site directed irreversible inhibitors" of DHFR (for a more exhaustive treatment of this subject, the reader is referred to his excellent monograph bearing a similar title), leading to the synthesis of several potential folate antagonists, at least one of which is currently a candidate for clinical trial. Compared with the prevailing empiricism in drug design, Baker's approach is original, enlightening, refreshing, and by far the most intellectually appealing. The enormity of the problem of design of folate antagonists for cancer chemotherapy can be readily grasped by the fact that, of the hundreds of new compounds synthesized by Baker for this purpose, few have lived up to expectation, and fewer still have even been considered for clinical trial. It must be realized that in the absence of any information on the structure of DHFR, Baker's model of this enzyme is no more than an educated guess at best. His initial decision to base his work on drug design by *in vitro* assaying drug effect on target enzyme and purposely to disregard the relevant pharmacokinetic factors tends to reduce the problem to a virtuosic synthetic exercise purely for the discovery of a powerful *in vitro* inhibitor of DHFR rather than a more clinically useful drug. Naturally, Baker was fully aware of these critical factors; nevertheless, even for a great sage, the temptation to be completely wrapped up in his own attractive theory may have occasionally become irresistible.

Another masterly dissertation of particular interest to medicinal chemists is that by C. Hansch, an equally well-known, ingenious drug designer and structure-activity relationship (SAR) researcher. Hansch has now incorporated into his extensive series of studies about 20 of Baker's 2,4-diamino-1,3,5-triazine inhibitors of DHFR. To appreciate the refinements which he has introduced into his "linear free energy equations," the reader should familiarize himself with an earlier publication by Hansch, namely, ref 18 cited in the current paper. Referring to this prior paper, he has used a "dummy parameter D" to replace the customary σ, the so-called extrathermodynamic constant for electronic effects of substituents. The exact physicochemical significance of D remains obscure, but Hansch thinks it has to do with the "stereoelectronic character" of a substituent. Perhaps what is really meant here is that D describes the extent of p–π overlap between N^5 and its substituents. If so, the validity of the contention could be tested with compounds in which N^5-phenyl group bears bulky ortho,ortho′ substituents. Inevitably, attempts to improve correlation by the addition of extra parameters cannot succeed except at the expense of elegance and aesthetic appeal. In his beautiful paper, Hansch has included only Baker's triazines; how well this theoretical treatment is applicable to folate antagonists of the pteroyl-glutamate type remains to be seen. A further comment concerns the biological data on which Hansch bases his structure–activity analyses. Any variability and divergence in the bioassay procedure would adversely influence the outcome of his work. In any event, unquestionably he has made unparalleled original contributions to drug design and SAR research, and I am anxiously looking forward to the complete rational and even computerized design and synthesis of more efficacious folate antagonists as cancer chemotherapeutic agents, a concept recently advocated by the same author [C. Hansch, *Cancer Chemother. Rep.*, **56**, 433 (1972)]. In this connection, I should like to draw the attention of interested readers to an admirable review on SAR of folate antagonists by J. A. R. Mead, *et al.* [*Cancer Chemother. Rep., Part 2*, **1**, 273 (1968)].

Other excellent articles included in the monograph are, to mention but a few, a competent review of the metabolism of folate antagonists, a discussion of a computer model for tissue distribution studies of these compounds, and a superb paper on the membrane transport of MTX and derivatives.

I am most favorably impressed by the overall quality of the papers, unusual for a monograph by some 90 authors. The editor deserves full credit for producing such an exceptionally fine book within a year of the conference. The price is relatively stiff, but by becoming a member of the N. Y. Academy of Sciences, the reader receives this and other equally valuable monographs absolutely free, a point worthy of serious thoughts. Although not in the same category as Blakley's monumental book, "The Biochemistry of Folic Acid and Related Pteridines," this is an up-to-date reference and an indispensable overview of the folate antagonists field. I highly recommend it to medicinal chemists in general and cancer chemotherapists in particular.

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Virus-Cell Interaction and Viral Antimetabolites. Edited by D. Schugar with 27 contributors. Vol. 22 of Federation of European Biochemical Societies, Proceedings of the Seventh Meeting, Varna, Bulgaria, 1971. Academic Press, New York, N. Y. 1972. viii + 231 pp. 16 × 23.5 cm. $4.00.

This book is the product of a symposia held to discuss the above topic. The subject is extremely current and of interest to a broad segment of the scientific community. The book is well organized and includes many of the current leaders in their particular fields as its contributors. Many of the topics discussed are not mentioned elsewhere in print and therefore make the book unique.

Since a majority of the material presented deals with the interaction of RNA tumor viruses (oncogenic virus) and host cells, it would have been a welcome inclusion to have data concerning the newly isolated human candiate oncorna viruses.

Topics of current importance such as reverse transcriptase, effects of Rifamycin and 5-iodo-2-deoxyuridine, temperature-sensitive mutants of Adenovirus, and effects of interferon are handled skillfully and in an understandable manner for those not completely conversant in these fields.

Another major contribution of the book is the reference section which appears after each of the 11 topics presented. These serve as a possible expansion of knowledge to the reader who wishes more details than are provided in the book.

The book is well edited and amply illustrated. I recommend it to those interested in the subject covered.

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Electrochemistry: Calculations, Simulations, and Instrumentation. Edited by James S. Mattson, Harry B. Mark, Jr., and Hubert C. MacDonald, Jr. Marcel Dekker, New York, N. Y. 1972. 466 pp. 6.5 × 9 in.

This volume, the second of a series, is a valuable addition to the library of any electrochemist. It is rich in details and practice of modern electrochemistry. There is a particularly strong emphasis on the use of small computers, both for data analysis and experimental control. The individual chapters, contributed by experts in their respective areas, are well written and each stands on its own to a large degree.

This review, however, is not for electrochemists but for medicinal chemists and their cohorts. As a former electrochemist turned neurochemist or neuropharmacologist (or something, I hope), this reviewer can wear two hats while evaluating this book. From the electrochemist's viewpoint, it is excellent. From the medicinal chemist's viewpoint, I can see very little of interest in this volume.

While I firmly believe that medicinal and biological chemistry in general can profit greatly from the know-how of modern electrochemistry, this book will help very little in that direction. Most medicinal chemists simply will not have the background to benefit from this material. This is in no way intended to be disparaging toward medicinal chemists–rather, the book is written at a level of sophistication aimed toward experts or at least those with an intense interest in electrochemistry. Only one or two chapters are of an introductory nature or are general enough to be of value to those outside the field. Osteryoung's introduction to the on-line use of computers in electrochemistry is a delight to read and can be appreciated by all. I cannot imagine any medicinal chemists being interested in reading much further in the book.

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