

the products with authentic standards<sup>1</sup> by TLC, GLC, and GLC-mass spectrometry led to the identification of three of the four zones. A parallel study was done with rat liver microsomes for comparison purposes (Tables I and II). The identification of zone four rests mainly on its TLC mobility, because it was not possible to isolate sufficient pure material for GLC-mass spectrometry analysis. A possible metabolite, 6 $\beta$ - $\Delta^1$ -tetrahydrocannabinol, can be excluded on the basis of its markedly different TLC mobility from that reported (8).

It can be seen from the results that mouse liver microsomes metabolize  $\Delta^1$ -tetrahydrocannabinol even more extensively than the analogous rat system. The most notable difference is the greater proportion of 6 $\alpha$ -hydroxy- $\Delta^1$ -tetrahydrocannabinol versus 7-hydroxy- $\Delta^1$ -tetrahydrocannabinol. Concurrent results from another laboratory have also shown that 6 $\alpha$ - and 7-hydroxy- $\Delta^1$ -tetrahydrocannabinols are major products when  $\Delta^1$ -tetrahydrocannabinol is incubated with mouse liver microsomes<sup>2</sup>. Since both metabolites are psychoactive (7), evidence for their presence in a particular species is of importance in interpreting pharmacological studies with  $\Delta^1$ -tetrahydrocannabinol. The production of 6 $\alpha$ -hydroxy- $\Delta^1$ -tetrahydrocannabinol becomes of equal interest to that of 7-hydroxy- $\Delta^1$ -tetrahydrocannabinol since the former has been tentatively identified in human plasma (8).

Our results may also help to establish the nature

of one unknown metabolite from rat lung and liver reported by Nakazawa and Costa (9). While we have not been able to make a direct comparison, it seems likely that their  $R_f$  0.48 metabolite is 6 $\alpha$ -hydroxy- $\Delta^1$ -tetrahydrocannabinol, since both our and their rat liver experiments produced only one substance intermediate in mobility between  $\Delta^1$ -tetrahydrocannabinol and 7-hydroxy- $\Delta^1$ -tetrahydrocannabinol.

(1) S. H. Burstein, in "Marihuana: Chemistry, Pharmacology, Metabolism and Clinical Effects," R. Mechoulam, Ed., Academic, New York, N.Y., 1973, chap 4. (See chap. 1 for a discussion of nomenclature.)

(2) A. Ryrfeldt, C. H. Ramsay, I. M. Nilsson, M. Widman, and S. Agurell, *Acta Pharm. Suecica*, **10**, 13(1973).

(3) E. W. Gill and G. Jones, *Biochem. Pharmacol.*, **21**, 2237(1973).

(4) R. Q. Freudenthal, J. Martin, and M. E. Wall, *Brit. J. Pharmacol.*, **44**, 244(1972).

(5) H. D. Christensen, R. I. Freudenthal, J. Gidley, R. Rosenfeld, G. Boegli, L. Testino, D. R. Brine, C. G. Pitt, and M. E. Wall, *Science*, **172**, 165(1971).

(6) S. Burstein and D. Kupfer, *Ann. N.Y. Acad. Sci.*, **191**, 61(1971).

(7) Z. Ben-Zvi, R. Mechoulam, H. Edery, and G. Porath, *Science*, **174**, 951(1971).

(8) M. E. Wall, D. R. Brine, C. G. Pitt, and M. Perez-Reyes, *J. Amer. Chem. Soc.*, **94**, 8579(1972).

(9) K. Nakazawa and E. Costa, *Nature*, **234**, 48(1971).

Zvi Ben-Zvi  
Sumner Burstein<sup>x</sup>  
John Zikopoulos

Worcester Foundation for  
Experimental Biology  
Shrewsbury, MA 01545

Received February 15, 1974.

Accepted for publication May 6, 1974.

Supported by National Institute of Mental Health Grant DA-00298.

<sup>x</sup> To whom inquiries should be directed.

<sup>1</sup>Labeled and unlabeled  $\Delta^1$ -tetrahydrocannabinol as well as samples of the metabolites were obtained from the National Institute of Mental Health.

<sup>2</sup>Professor S. Agurell, Faculty of Pharmacy, Stockholm S-113 86, Sweden, personal communication.

## BOOKS

### REVIEWS

**Selective Toxicity**, Fifth Edition. By ADRIEN ALBERT. Chapman and Hall, London, England, 1973. 597 pp. 15 × 23 cm. Price £7.

"Selective toxicity" is defined by Adrien Albert as "the injury of living matter without harming another kind with which the first is in intimate contact." Those organisms (including humans) that are not injured are referred to as "economic species," while those which are harmed are classified as "uneconomical species." Examples can be given where chemical agents that are toxic to one type of plant have little effect upon other plants growing on the same plot of land. In the animal world, insecticides are so chosen to bring death to insects and pest without harming useful animals and plant life. Selective toxicity as interpreted by Albert is applicable to all drugs since they will alter one or more physiological or biochemical processes to help bring about a state of normalcy. For a large number of drugs the toxic effect is revers-

ible, for example, the general anesthetics, sedatives, and drugs used to relieve pain. Other drugs such as the antibiotics bring about a nonreversible toxic effect, in this case to the noneconomic species, the bacteria, without harm to the host (economic species).

In an oversimplification, selective toxicity may be considered a general approach of helping rid the world of undesirable organisms through chemical agents while permitting useful ones to flourish. Even though the mechanisms by which one chemical agent can harm one species while having relatively little effect upon another are complex and often unknown, Albert approaches the subject in a very methodical and deliberate manner and bases his thesis, as in the past, upon the chemical structure and physical properties of the agents.

The present edition is the fifth and when compared to the first (1951) and second editions (1960) monumental growth of the book is apparent. For example, the 1960 issue was a mere 233 pages versus the present 597 pages. While the 1960 edition was a relatively breezy approach to the subject which could be read with

comfort, the present volume is sometimes hard to read and often requires great care. Yet this should be expected because of the advances made in therapy, biochemistry, pharmacology, and the general knowledge explosion. The ability of one author to compose a book such as the present edition is truly amazing. Its value as a text in medicinal chemistry as well as a reference source for advanced students interested in the first principles of drug and chemical actions is outstanding.

Albert has divided his book into two parts. The first part deals with topics of general interest to the reader such as toxicity in the service of people, differences in distribution—the first principle of selectivity, comparative biochemistry—the second principle of selectivity, and comparative cytology—the third principle of selectivity. Part I ends with chapters devoted to chemotherapy—history and principles, and pharmacodynamics.

Nine chapters comprise Part II of the book. Topics in these chapters are addressed directly to the relationship between structure and physicochemical properties of chemical agents primarily having economic value. This part of the book starts with a chapter on the nature of chemical bonds, adsorption, and the influence of methyl groups on biological action and continues with other chapters on metabolites, ionization, metal-binding substances, the covalent bond in selective toxicity, steric factors, surface chemistry, free radicals, and ending with the last chapter devoted to biological activity unrelated to chemical structure.

Even though many readers may have the last edition and may be reluctant to spend more money on a new edition, it is advisable for them to examine the Fifth Edition since sufficient changes and updating of materials have taken place to justify obtaining the present edition.

I suspect that this book will have the greatest value to pharmacy students who are required to have substantial scientific background in the action of drugs and useful chemicals. Even though many schools have played down the "science" in recent years, those still interested in educating the pharmacy student will find this book an excellent companion which can supplement lectures in medicinal chemistry and pharmacology. Graduate students in toxicology will also benefit from having this book in a handy place when a knowledge of first principles of chemical actions on biological systems is desired.

*Reviewed by John Autian  
College of Pharmacy  
University of Tennessee  
Medical Units  
Memphis, TN 38163*

---

**Pharmacology: Drug Actions and Reactions.** By RUTH R. LEVINE. Little, Brown, Medical Division, 34 Beacon St., Boston, MA 02106, 1973. 412 pp. 16 × 24 cm. Price \$9.50.

This is a superb little book that should be read by all students interested in the actions of drugs. It should be especially useful to graduate students in pharmacology and to students of medicine and pharmacy.

The style is clear, simplified, and easy to read. The illustrations are generally good but not numerous. The suggested reading, synopses, and introductory paragraphs are well done (the reader is told what will be discussed, it is then discussed, and it is summarized). The glossary is adequate. Italicization of key words and phrases will be appreciated by students.

The section on "The Heritage of Pharmacology" is truly superb and concise. The development of the receptor concept is good.

Some of the definitions offered (Chapter 2) are at variance with those commonly accepted. For example, *pharmakon* is Greek for drug and *toxicon* is the word for poison. Dr. Levine lists *pharmakon* as meaning a poison. The definition of toxicology is very restrictive.

Notably absent were the following: a discussion of the Henderson-Hasselbalch and Jacobs equations; first-order (or apparent

first-order) kinetics; and a discussion of the measurement of acute toxicity ( $LD_{50}$  and the methods used in calculating it).

This fine little book may be considered a concise, simplified edition of the classic work by Goldstein *et al.* For the beginning student, it will be much easier to comprehend and should excite the student to "read on."

Dr. Levine should be complimented on this fine contribution.

*Reviewed by J. F. Borzelleca  
School of Pharmacy  
Medical College of Virginia  
Richmond, VA 23219*

---

**Photochemistry, Volume 4.** Specialist Periodical Report. Senior Reporter, D. BRYCE-SMITH. The Chemical Society, Burlington House, London W1V 0BN, England, 1973. 979 pp. 15 × 22 cm. Price £16.

This latest volume on photochemistry in a well-known series provides review coverage of the period July 1971 through June 1972. It contains a massive amount of information on both theoretical and practical aspects of photochemistry. The importance of modern photochemistry is evidenced by the scope and number of publications covered in this volume.

The largest number of references is found in Part I, "Physical Aspects of Photochemistry," dealing with theory and instrumentation, *e.g.*, laser technology, as well as photophysical processes in condensed and gas phases. Part II, "Inorganic Photochemistry," treats the photochemistry of water, the hydrated electron, metal complexes, and inorganic solids to name but a few.

The largest section of the book, "Organic Aspects of Photochemistry" (Part III), is probably of major interest to persons involved in the pharmaceutical sciences. One is struck first of all by the extent of photochemical studies performed with organic compounds and the very practical implications for the synthetic chemist. Discussions are presented of papers dealing with classical Norrish-type reactions; synthesis of cyclobutanols and aziridines; a multitude of addition, isomerization, and rearrangement reactions of unsaturated compounds; extensive photochemistry of heterocyclic compounds including nucleotides,  $\beta$ -carboline alkaloids; reduction of haloaromatic compounds; *etc.* The arrangement according to both class of compounds and type of reaction sometimes appears confusing, but it is heartening to see the advances that have been made in systematizing organic photochemistry. The final section, "Polymer Photochemistry," treats both photopolymerization and photodegradation reactions. Current concern about the removal of solid and atmospheric pollutants should increase future research efforts in photochemical methods of degradation, not only of polymeric materials but also of simpler substances such as chlorocarbon insecticides (p. 618).

As with any volume of the review type some of the material presented is given detailed treatment while some is presented in a very sketchy fashion. One drawback of the present volume is repetition. For example, the irradiation of 5-bromopyrimidine in methanol is discussed on both pages 666 and 804, and the photo-reaction between cytosine and 4-thiouracil (p. 549) is repeated on p. 821. Elimination of these and other instances of duplication may have permitted a lower-priced book.

Overall, the volume is a useful, well-organized review of the state of photochemistry through June 1972. Anyone interested in keeping up-to-date in modern photochemistry (a difficult task in any branch of science) may wish to be able to refer to it in a library. Otherwise, the price will prohibit a personal copy to anyone but the practitioner of photochemical methods.

*Reviewed by George E. Wright  
Department of Medicinal Chemistry  
School of Pharmacy  
University of Maryland  
Baltimore, MD 21201*