F. Christine Brown
Ph.D.

Associate Professor of Biochemistry
Research Associate in Psychiatry
Brain Research Institute
University of Tennessee Medical Units
Memphis, Tennessee

HALLUCINOGENIC DRUGS

Written to provide further knowledge of the chemistry of hallucinogenic drugs—focusing primarily on the chemistry which is relevant to the pharmacological and psychological effects. The hallucinogens are divided into classes based on chemical structure, describing in separate chapters lysergic acid compounds (LSD in the prototype), the indoles (psilocybin), phenylethylamines (mescaline), cannabinoids, and others. The best known derivatives of each class are discussed in some detail, with the relationships between compounds of similar and dissimilar structures compared.

HALLUCINOGENIC DRUGS

Publication Number 825

AMERICAN LECTURE SERIES®

A Monograph in

The BANNERSTONE DIVISION *of*
AMERICAN LECTURES IN LIVING CHEMISTRY

Edited by

I. NEWTON KUGELMASS, M.D., Ph.D., Sc.D.

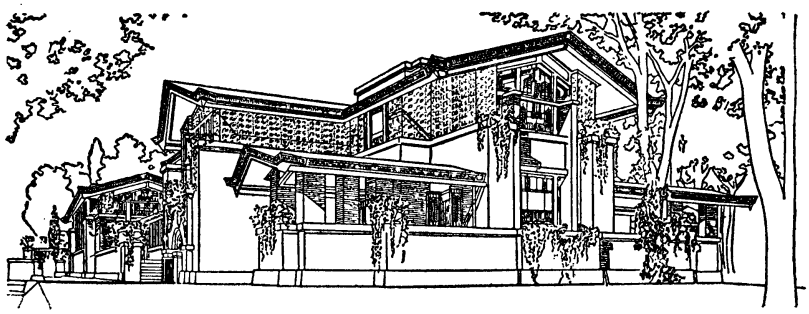
Consultant to the Department of Health and Hospitals
New York, New York

Hallucinogenic Drugs

By

F. CHRISTINE BROWN, Ph.D.

Associate Professor of Biochemistry
Research Associate in Psychiatry
Brain Research Institute
University of Tennessee Medical Units
Memphis, Tennessee



CHARLES C THOMAS • PUBLISHER
Springfield • Illinois • U.S.A.

Published and Distributed Throughout the World by
CHARLES C THOMAS • PUBLISHER
BANNERSTONE HOUSE
301–327 East Lawrence Avenue, Springfield, Illinois, U.S.A.
NATCHEZ PLANTATION HOUSE
735 North Atlantic Boulevard, Fort Lauderdale, Florida, U.S.A.

Library of Congress Catalog Card Number: 74-165878

Printed in the United States of America
CC-11

FOREWORD

OUR LIVING CHEMISTRY SERIES was conceived by Editor and Publisher to advance the newer knowledge of chemical medicine in the cause of clinical practice. The interdependence of chemistry and medicine is so great that physicians are turning to chemistry, and chemists to medicine in order to understand the underlying basis of life processes in health and disease. Once chemical truths, proofs and convictions become sound foundations for clinical phenomena, key hybrid investigators clarify the bewildering panorama of biochemical progress for application in everyday practice, stimulation of experimental research, and extension of postgraduate instruction. Each of our monographs thus unravels the chemical mechanisms and clinical management of many diseases that have remained relatively static in the minds of medical men for three thousand years. Our new Series is charged with the *nisus élan* of chemical wisdom, supreme in choice of international authors, optimal in standards of chemical scholarship, provocative in imagination for experimental research, comprehensive in discussions of scientific medicine, and authoritative in chemical perspective of human disorders.

Dr. Brown of Memphis unravels the dim haze of mystery on the psychoactivity of hallucinogens with enchantment in its pursuit. These "mind drugs" produce varied experiences—psychotic, psychodynamic, cognitive, aesthetic, mystical to ease the uncertainties of the day and avoid psychic pain, to achieve pleasure, to find faith, to reach experiential transcendence, to seek the imagery of rebirth. Once the quest is on, the individual relinquishes the core of his existence, his individuation, for the potion becomes the master. First he takes the drug, then the drug takes him. Once the Rubicon is crossed, the barriers are gradually let down for destruction.

An hallucinogen interferes with brain metabolism producing uncontrolled stimulation and altered perception. It is mind-expanding or psychedelic reducing the perceptual filter to give the user a "trip." He experiences distortion of time, space and colors and hears colors and sees colored sounds. There is regression into the past and the individual feels as if he is coming out of his body experiencing vivid revelatory hallucinations. The "mind drugs" serve the new mood for mysticism and exploration of internal space.

Man has been an inveterate experimenter with chemicals, usually derived from plants, that made him happier or livlier or altered his perception and awareness. Natural hallucinogenic drugs like marijuana, hashish, and peyote have been known since prehistoric times and used in religious rites down to the present. Artificial hallucinogens like LSD and THC have become well known for two decades. The same drug in the same dose in the same person may produce very different effects, according to the events which precede or follow a particular medication. Hallucinogens are illegal because of their presumed harmful effects. Unlike opium derivatives, none is addicting; unlike barbiturates, none is a cerebral depressant. Like sedatives and anesthetics, they alter subjective states of awareness pleasurably in mind-expanding sensations. They may cause temporary psychoses, dreamy states and delusional withdrawals from reality which may produce permanent damage. Nevertheless, the hallucinogens constitute behavior-control devices for the future once their specificity and selectivity are delineated. The hallucinogen is like the finger of God, it can slake and it can smite.

What is this I hear of sorrow and weariness
Anger, discontent and drooping hopes?
Degenerate sons and daughters
Life is too strong for you
It takes life to love Life.

I. NEWTON KUGELMASS, M.D., Ph.D., Sc.D., *Editor*

PREFACE

Part of my duties at the University of Tennessee Medical Units is to participate in the teaching of freshman medical students. For the past two years, several groups of young men have worked with me in a varied and continuing study of hallucinogenic drugs. Together we have examined the literature; the history, biogenesis, pharmacology, toxicity and psychoactivity of these materials have been explored. We have probed the chemical properties, searching for a clue to the mystery of their psychoactivity. Also, we have discussed, sometimes objectively, but at times with individual personal commitment, the social and cultural ramifications of drug-taking.

In this monograph, I have tried to retain, or rather, to capture, some of the essence of those sessions; the casual concern, the exuberance, the willingness to accept and/or to modify reality, the disappointments that so often accompany knowledge, especially when the latter interferes with the stuff from which dreams are made, and, above all, honesty. That is not to say that all of my own personal bias and opinions as related to drug-taking and the effects thereof have been excluded. Bidden or not, bias and opinion have an insidious way of creeping into every thoughtful endeavor. But I have tried to be honest with myself and the reader. In those areas where opinions, as opposed to a physical property such as say, aqueous solubility, may influence the evaluation of a drug or the response to a drug, I have tried to present the various views. However, I may have made no effort to conceal my own evaluation of the concept under discussion.

As for organization, the book has been built around the chemical distinctiveness of the drugs. Medically trained individuals, in my opinion, tend to shy away from chemistry, par-

ticularly if it appears to be irrelevant to a working concept. The key word, of course, is *relevance*. Students readily shed their timorous regard for the chemistry of drugs when confronted with the molecular intrigue built into each compound—and to the necessity for knowing that the intrigue is there. One can almost see the mental machinations evoked by the realization that substances such as psilocin and serotonin are chemically very similar compounds. Using the chemical structure as a base, the dosage, pharmacological, biochemical, and psychological properties can be more meaningfully discussed.

For information I have relied extensively on literature reviews and published symposia. In the past five years, these have appeared in respectable numbers in the literature of pharmacology, biochemistry, psychiatry, as well as in the neurosciences, psychopharmacology, and so forth. Thus, it is possible to derive a broad based view of drugs and attendant problems. For the most recent developments of the past year or two, journals, periodicals and books have been searched for current research results and articles of topical interest.

The author is indebted to several people for help in the preparation and appraisal of this manuscript. Dr. W. G. Struve, Assistant Professor of Biochemistry, and Dr. A. O. Battle, Associate Professor of Clinical Psychology at the University of Tennessee Medical Units read the manuscript and offered constructive suggestions for improving it. I am also indebted to the nimble fingers of Mrs. W. G. Struve (Nancy) for typing the final draft. Lastly, I must thank Mrs. Jerry Defoor and Palmer Gordon for many hours of tedious proofreading. Without the help of these generous people, the task of putting this book together would have been much more difficult.

F. CHRISTINE BROWN

CONTENTS

		Page
Foreword		v
Preface		vii
Chapter		
I.	General Considerations	3
II.	Phenylalkylamines: Mescaline and Amphetamines	11
	Phenylethylamines	11
	Phenylisopropylamines	19
III.	Lysergic Acid Derivatives	36
	Ololiuqui	64
IV.	The Indoles	78
	Indole Alkylamines	79
	The β-Carbolines	88
	Iboga Alkaloids	92
V.	Marihuana	99
VI.	Piperidyl Benzilate Esters and Related Compounds	123
	Sernyl	131
VII.	Some Minor Hallucinogens	137
	Fly Agaric	137
	Nutmeg	139
	Kava	143
Index		149

HALLUCINOGENIC DRUGS

Chapter I

GENERAL CONSIDERATIONS

THERE ARE MANY substances which will, if taken in the appropriate quantities by normal subjects, produce distortion of perception, vivid images, or hallucinations. Most of these compounds will produce powerful peripheral as well as central nervous system effects. A few agents are characterized by the *predominance* of their actions on mental and psychic functions. This group of compounds has been called the *hallucinogens.* Several other terms have been used: *psychotomimetics, psycholytics, psychotogens,* the theatrical-sounding *phantastica,* and *psychedelic.* Of these titles, psychedelic, a term coined by Osmond[1] meaning "mind manifesting" and which has been called an "etymologically impossible word" by Schultes,[2] is the most widely known to the general public. In recent years, the term has become a synonym for the morals, mores, and actions resulting from the use and misuse of the most famous of the hallucinogens, LSD. Psychotomimetic, which means *mimicking psychoses,* was introduced to describe the capacity of these agents to induce a so-called model psychosis. Because of the diverse nature of the symptoms observed under different conditions of administration and dosage, the variety of chemical structures included, and a general lack of knowledge as to the underlying mechanisms involved in the physiological and psychological effects, none of the names suggested to date are adequately descriptive. This writer prefers the term hallucinogen for mostly negative reasons. It does not imply any knowledge, or suggest a hypothesis, as to how, why or where, these agents elicit the observed effects, but it does describe one specific property which most of them have in common.

Classification of the Hallucinogens

The major hallucinogens of current interest may be classified into five groups of chemically distinct compounds and a sixth group composed of substances of diverse chemical identities:

1. lysergic acid derivatives
2. indolealkylamines
3. phenylethylamines
4. piperidylbenzilate esters
5. cannabinoids
6. other

Except for the benzilate esters and a related group of compounds, the phenylcyclohexyls, which are products of a more practical "manifestation of mind," synthetic organic chemistry, drugs representing all of these classes have been isolated from natural products. Most of the hallucinogens identified to date are alkaloids, that is, having alkaline properties. The one major exception is the cannabis group. Alkaloids are found abundantly in plants. Out of the total number of plant species, variously estimated to be from 400,000 to 800,000,[3] only about five thousand or so are known to be alkaloidal. Surprisingly few of these, about sixty, produce hallucinogens. Ethnobotanical researchers, who go into remote inaccessable areas of the world in search of rapidly disappearing primitive cultures, say that there are appreciable numbers of hallucinogenic plants still unknown to scientists.

Current interest in psychoactive compounds has stimulated an intense search for these unknown plants, and a closer look at the active ingredients of those that are known. Recent evidence[3] has shown that the active ingredients of fly agaric from the mushroom, *Amanita muscaria*, is not muscarine or bufotenine, both of which are present in small amounts, but muscimole, an unsaturated hydroxamic acid, and ibotenic acid. Although Hofmann and Tscherter[4] found lysergic acid derivatives in morning glory seeds, Cook and Kieland[5] isolated a glucoside from an extract (ololiuqui) of these seeds which is five times as active as the original extract. Thus, the list of