

Praise for *The Nature of Drugs*

“For those of us who were not fortunate enough to attend Sasha’s classes, this book is a fantastic second chance to learn from a brilliant, principled, courageous, idealistic psychedelic chemist whose creations were molecules for psychotherapy, spirituality and celebration, to help humanity wake up and save ourselves.”

— Rick Doblin, Ph.D.

Multidisciplinary Association for Psychedelic Studies (MAPS)
Executive Director

“Legendary chemist, nuanced psychonaut of molecular structure-activity relations, deep thinker on issues of societal policy, engaging storyteller, inspirational teacher, and all-around good human being—Sasha Shulgin takes us on an alchemical educational journey as if we were sitting there as students in the class from which this text arose. What a gift!”

— David E. Presti, Professor of Neurobiology, University of California, Berkeley

Author of *Foundational Concepts in Neuroscience: A Brain-Mind Odyssey*
and *Mind Beyond Brain*.

“If you’re curious about any drug, from caffeine to LSD, this is the book for you. What an absolute treat to learn from the best, to have Professor Shulgin as your personal instructor, with all of his charming, self-effacing asides and his witty encyclopedic knowledge on display.”

— Julie Holland, MD

Author of *Good Chemistry: The Science of Connection from Soul to Psychedelics*
Editor of *Ecstasy the Complete Guide* and *The Pot Book*

“These course lessons are pure Sasha: enthusiastic, surprising, tangential, goofy, and shockingly knowledgeable. But they also give us something that remains terribly rare, even at this late date: a kaleidoscopic approach to the problems and possibilities of drugs that is at once pragmatic, visionary, and genuinely inter-disciplinary. Once again, Shulgin proves himself a magnificent spirit as well as a magnificent mind. I learned a lot, and enjoyed myself tremendously.”

— Erik Davis

Author of *High Weirdness: Drugs, Esoterica, and Visionary Experience in the 70s*

© Copyright Alexander 'Sasha' Shulgin 2021
Foreword © copyright Mariavittoria Mangini 2021
All rights reserved.

No part of this publication may be reproduced, stored in any retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise without the prior permission of the publisher, except for the quotation of brief passages in reviews.

Co-published by:
Transform Press | P.O. Box 1152, Berkeley, CA 94712
Synergetic Press | 1 Bluebird Court, Santa Fe, NM 87508
& 24 Old Gloucester St. London, WC1N 3AL England

Library of Congress Cataloging-in-Publication Data is available.

ISBN 9780999547212 (hardcover)
ISBN 9780999547229 (ebook)

Cover design by Ann Lowe & Amanda Müller
Book design by Brad Greene
Managing Editor: Amanda Müller
Transcribed by Melitta von Abele
Transcription Corrections: Keeper Trout
Printed by -----

TABLE OF CONTENTS

Acknowledgements	<i>xi</i>
Publisher's Note ~ by Wendy Tucker	<i>xiii</i>
Foreword ~ by Mariavittoria Mangini	<i>xv</i>
Introduction ~ by Keeper Trout	<i>xxiii</i>

LECTURE 1: **Course Introduction**

Overview and Introductory Discussion

Sasha's Introduction

“What is a Drug?”

Definitions from Lectures 1 and 2

LECTURE 3: **The Origin of Drugs**

Overview

Opening discussion: Sasha's view on drugs, laws, power,
and social control

The Origin of Drugs

Human Development and Origins

Alchemy

Chemotherapy

The Origins of Drug Scheduling, Enforcement
and How Drugs are Scheduled

Definitions

LECTURE 4: The Plumbing of the Human Body 109

Overview

Pharmacokinetics and Pharmacodynamics

How Drugs Get into the Body

Drug Administration Methods

Biotransformation:

The Half-Life of Drugs in the Body

Metabolic Interactions of Drugs

LECTURE 5: More Body Plumbing & the Nervous System 141

Overview

Biotransformation Continued:

Absorption, Excretion, and Routes

Administration Methods and their Effects on Drugs

The Nervous System

The Central Nervous System

The Autonomic Nervous System

Nerves, Structure, and Function

LECTURE 6: Drug Action 195

Overview

Drug Treatment Categories

Sasha's Drug Treatment Classifications

Review of Drugs and The Nervous System

LECTURE 7: **Memory & State of Consciousness** 233

Overview

States of Consciousness

Memory

Changes in Consciousness without Drug Intervention

Mental Illness

LECTURE 8: **Research Methods** 265

Criminalistics and Drug Testing

Defining the Research Question

Devising a Hypothesis

Clinical Drug Trials

Human versus Animal Testing

Lecture 3 Notes, 1987

Reflections from a Former Student ~ by Leonard Pickard 319

Afterword ~ by Paul F. Daley 329

References 333

Index 335

PUBLISHER'S NOTE

This book is a time capsule.

When Sasha taught this class, computers were in use but most of his research was done through periodicals, journals, and books. He went to the library. You'll hear him referencing his favorite journals, and he will describe how to find the information desired, but of course this has changed a great deal since then. This is true too with the information he gives about patents and laws, it is not up to date.

We ask that you keep this in mind as you read this book, and to understand that regardless of these details, his advice and wisdom about *how to do research well* is still true. If Sasha were alive teaching this class today, he would probably tell people that they must be even more diligent than ever to weed through all of the misinformation there is on the internet. Research may be easier to do in some ways, but finding what is real and true takes more work, more skill, more objective and critical thinking, and is probably more difficult than before.

Enjoy this first volume of *The Nature of Drugs*!

— Wendy Tucker
Publisher, *Transform Press*
February 2021

FOREWORD

There are many aspects of Sasha Shulgin's life and work that will likely be familiar to readers of this book. His best-known works, *PiHKAL* and *TiHKAL*, written with Ann Shulgin, combine the stories of their courtship and marriage with chemical synthesis information from private notes on psychedelic compounds. Working in his lab, in a shed in the yard of the Shulgin Farm, his family home, Sasha independently created more than 200 psychoactive substances. Although his research papers describing the hundreds of unique chemical compounds that he synthesized have been widely published, and his work is of unquestioned importance, his research was not subsidized by a university, a government research facility or an industrial sponsor. Instead, he supported his work and maintained his independence from potentially censorious influences by consulting, lecturing and teaching. The Farm today is the repository of a treasure trove of research documents and reports, lectures, journals, letters, and photographs that comprise Sasha's scientific library and personal papers, which are now being explored and digitized. This book, which represents the transcripts of the first semester of a pharmacology class taught by Sasha in 1987, is a part of that effort.

In approaching the material presented in *The Nature of Drugs*, it is important to note that the social environment in which a contemporary reader encounters these lectures is significantly different from the one that prevailed when they were presented. In 1987, this country was in the midst of a moral panic about drug use. The use of plants and chemical compounds for the purpose of consciousness alteration was generally considered to be a criminal act. Although research indicated that many users of illegal psychoactive drugs were able to function effectively and undetectably in society, most public policy of that time presupposed that such use would inevitably have demonstrable negative consequences.

At the time that these lectures were presented, the popular and the legal formulations of the use of illegal drugs allowed, for the most part, for only two patterns: abstinence and abuse. Any illicit drug use was defined as abusive, and moderate use was believed to be an unstable pattern, which might at any time deteriorate into uncontrolled use or drug addiction. Studies of drug users often failed to differentiate between different patterns of use, employed imprecise and inaccurate terminology in describing levels of use, or made no attempt to describe patterns of moderate use. The majority of theories that explained drug use and described the drug user did so in such negative and pathological terms that it seemed mysterious that any drug users survived at all. Sasha was one of the minority of drug experts who recognized the existence of a large number of experimental or occasional users who did not present any serious problem in terms of morbidity and mortality. On the contrary, he understood that drug users might value their experiences for many different reasons that did not arise from pathology, and that most drug users do not become abusers or addicts.

Ironically, the existence of patterns of moderate use was most publicly recognized by William Bennett, “drug czar” of the Bush administration, who acknowledged the possibility that experimental, infrequent, or even regular non-compulsive use of illicit drugs might have few detectable effects on the health, work, families or social lives of some users. Nevertheless, in Bennett’s 1989 National Drug Control Strategy, he singled out these “non-addicted casual users” for his strongest opprobrium, calling them “potential agents of infection for non-users,” presumably because they did not fit his description of drug users as “inattentive parents, bad neighbors, poor students, and unreliable employees” whom no one would wish to imitate.

With the ascendance of political conservatism during the Regan administration, problems that might be associated with the use of prohibited drugs had come increasingly to be viewed as resulting from moral, spiritual or biological defects of individuals, rather than as the product larger of social or environmental problems. The remedy for these

dysfunctions was greater social control, as opposed to social welfare. Cultural conservatives determined that they could use drug prohibition as a legitimate source of control over unruly elements: minorities, youth, aliens and cultural liberals; the “dangerous classes” that seemed to be getting out of control in the 1960’s and 70’s.

Drug prohibition became a powerful exponent of the projects of the cultural right. It displaced concern for social conditions such as poverty, lack of educational opportunity, racism, unemployment, and a deteriorating social safety net; and concentrated explanation of them on the deficiencies and weaknesses of the affected individuals. For groups that were experienced by conservative elements in society as disorderly, rebellious, and disrespectful of authority, opposition to their non-conforming behaviors was seen as a reaffirmation of social hierarchies and traditional moral values. Control of the use of drugs that might be favored by these groups has been used to provide the justification for increased social control and drug prohibition has historically been allied with expressions of racial and ethnic intolerance.

Sasha challenged this prohibitionist stance both for provincialism that specified a limited range of acceptable interests and experiences and for paternalism that surrendered autonomous decision making in return for a promise of security and safety. He drew critical attention to the substitution of lies, distortions and fallacies for history and scientific evidence that was characteristic of legalistic views of drugs and drug use. By contrast, he offered potential drug users a singular position: learn the facts, then make an informed decision for yourself. Rather than trying to control citizens’ choices, or resorting to hyperbolic fear mongering, he advocated a pragmatic alternative: scientific and realistically grounded education. This was drug education that was not directed solely at prevention of use, but which also provided those who chose to use with information that encouraged moderation, appreciated the legal consequences and social realities of drug use, and was based upon science.

Much of this first series of lectures is devoted to Sasha’s view of teaching and learning. He encouraged students to listen to the emerging

“music” that the interplay of his planned lecture outlines, inquiries and offerings from class members, and his own stream of thoughts produced; and he discouraged excessive notetaking as a distractor from the experience of in-person interaction with the class material. He wanted students to get the feel of his work as a chemist, but also as a philosopher and an artist. Drugs, he claimed, were incidental to his presentation of ideas about free choice and informed citizenship. They provided an occasion for Sasha to talk about what he claimed really went on in this class: an experience of learning that was designed to equip us to have freedom of choice and to retain our personal power of discernment in our decisions and actions. Sasha was an early endorser of “just say know” as an alternative to “just say no.”

Those of us who were fortunate to spend time in conversation with Sasha can almost hear his voice as we read these transcripts. He was an engaging teacher, masterful and authoritative about his subject, but ready to acknowledge ambiguities and areas that were outside his expertise. He was quick to grant that there were exceptions to his expert knowledge and that ten percent of his ideas would be likely disproven. His expressed wish in these classes was for the students to listen to the “music” of chemistry, which he saw as a creative exercise.

The incontestable principles of chemical structure served as a launching point for discussions about societal issues and controversies. In this series of lectures, which was intended for a general audience with no particular background in chemistry, Sasha prepared his listeners for the detailed discussions of specific drugs that would be presented in later classes. He covered basic anatomy and neuroanatomy, physiology and neurophysiology—our “plumbing and wiring” as he called them—pharmacological concepts such as pharmacokinetics and pharmacodynamics, definitions used to describe drugs and their effects, and a chronology of drug law and policy. By introducing the pharmacokinetic processes that explain the way that the body reacts to drugs and the pharmacodynamics of receptor effects and chemical interactions, Sasha opened a greater access to wide-ranging discussions of drug action for students who might

lack a background in these areas. More importantly, these lectures provided an opportunity for Sasha to present his opinions, convictions and principles in a context that attracted students with an interest in the role of psychoactive substances in human experience.

Sasha's teaching sometimes followed an outline or notes and sometimes, by his own admission, "just rambled around." In this lecture series, he laid the groundwork for further explorations that would come later, equipping his audience to participate with him in some wide-ranging conversations about individual drugs, what they do, and how we think and legislate about them. In order to do this, Sasha presented foundational knowledge that would permit his students to formulate pertinent questions and to follow him in his rambles. This background of understanding was meant to allow class time to be an interactive learning environment, where both students and instructor could engage creatively with the subject matter. Sasha used a broad definition of "drugs" which included "those things that influence a living organism or behavior," and he provided a picture of where drugs come from, and where they go, their actions, their risks, and their virtues. This became the basis for his later lectures not only on specific drugs, but also on topics that relate to a "wilder territory" that embraces as drugs such things as smog, radioactivity and pesticides.

The importance of Sasha's digressions and asides can't be overestimated. He provides practical examples that illustrate important concepts in a way that is in keeping with his position about note taking—that it distracts from listening appreciatively to the material being presented. He uses his position as an experienced researcher to discourage attempts to "prove" a hypothesis, and to remind his students that science advances by discovering that previous hypotheses are incorrect. He emphasizes the importance of asking the appropriate research question, and of designing inquiry as a quest to disprove hypotheses, since an experiment that proves a hypothesis is impossible to devise. He also delves into areas of philosophy and policy, and gives invaluable advice about the nature and conduct of research. Sasha was acutely aware of

the way that powerful persons, governments and agencies may be more committed to avoiding any admission of error than to moving from ignorance to enlightenment.

Sasha's comparison of drug education to sex education gives a hint of the perspective that led him to describe his chemical diagrams as "dirty pictures." The idea of both is to equip the listener to make informed decisions when the opportunity and the inclination to engage in certain behaviors may coincide. He was not reticent about including his views about social ethics in his lectures, but he did not advocate for or against drug use. He refuted the conventional ideas about abuse of drugs that define "abuse" as use of any forbidden drug, lack of permission from a specific professional prescriber for use, acquisition of drugs through unsanctioned channels, or use of drugs in ways that may introduce an element of danger. Sasha held to a definition of drug abuse that has nothing to do with illegality or medical supervision: as long as drugs can be used in ways that don't interfere with social functioning or mental and physical health, their use is not here considered to be abuse. In this more complex view of what constitutes abuse, the relationship of an individual to a substance is the crucial concern.

In order to have a foundation for following Sasha's lectures, and to keep up with his observations, stories and replies to their individual inquiries, students were encouraged to use the class' textbook to gain a basic vocabulary and understanding of the various kinds and classes of psychoactive drugs. The textbook, *From Chocolate to Morphine*, by Andrew Weil and Winifred Rosen, was first published in 1983, a few years before these lectures were presented. It is still in print almost 40 years later, and the ideas that made it an obvious choice for Sasha to select have come to enjoy greater acceptance: that the desire to alter consciousness is an innate, normal human drive, and that problems with drugs arise from poor relationships with drugs, not from the inherent characteristics of the drugs themselves.

At the present moment, Sasha's devotion to the presentation of truths backed up by scientific and historical evidence presents a refreshing

contrast to the encroachments of the current war on science. He saw himself as a truth seeker, rather than an advocate for or against drug use, and his work is an example of a cognitive lust: an intense desire to learn and know everything that there is to know about a fascinating subject. In his case, the inspirations for this enthusiasm were drugs that could cause not only visual and sensory changes, but could also modify and influence brain function. His interest was in drugs that “turn the mind;” psychotropic substances that can cause changes in perception, attitude, or point of view, and sometimes expand one’s mental and emotional horizons or provide access to one’s interior universe.

Sasha could be persuaded to admit that he was an alchemist. He approached chemistry as a sacred art and was mindful of the way in which the practical and the philosophical, the esoteric and exoteric, intersected in his work, as they did in classical alchemy. Historically, only a few practitioners of the arts he practiced rediscover this ancient truth. He viewed alchemy as a form of meditation, and chemistry as an art that was exactly like the composition of music, or the creation a painting: the putting of things together that had never been together before.

Sasha’s practice was informed by the realization that the essential alchemical work was to understand oneself. While he delighted in the practical work of the laboratory, he recognized that the transmutation that is sought in the alchemical quest is a spiritual regeneration of the practitioner, in an evolution from ignorance to enlightenment. He was grounded in the real and tangible but respectful and curious about the mystical and intangible. Sasha mused about the possibility of embedding one’s character in the substances that one works with, in a way that could be recognized by others. Beyond earth, water, fire and air, the elements of which everything is made, he was curious, as were the classical alchemists, about the quintessence, the fifth element, the spirit in matter, the soul that puts all the rest into place. In his work, Sasha Shulgin was able to achieve one of the goals of classical alchemy: to manifest spiritual forces for transformation in a material form. This class was a vehicle that he used to expose his audience to the ideas that shaped his work, and

THE NATURE OF DRUGS

which lent a quintessential character to the substances that he created and synthesized. For us who have had the benefit the transformative power of Sasha's discoveries and innovations, these lectures give a unique glimpse of his remarkable mind at work.

— Mariavittoria Mangini, PhD, FNP
Cofounder, Women's Visionary Council
December 2020

INTRODUCTION

What you are about to read is much more than a series of class notes, it is a taste of Sasha at his most entertaining. The Nature of Drugs was a very popular class taught at SFSU by Sasha (Alexander T.) Shulgin. This book was from one of those classes, recorded in 1987. These recordings have been transcribed to enable the experience of being in his class, to get a taste of Sasha's wildly free-form and fast paced lecturing and speaking style.

Despite rolling through technical subjects such as pharmacology in general, pharmacodynamics, pharmacokinetics, metabolism, excretion, toxicology, and forensics; this was an introductory level course aimed at students who had no background in chemistry, and required no other prerequisites. This makes what Sasha wants to say very accessible to anyone. Sasha loved teaching this class because of the opportunity it provided him to share, not only the core material, but a bit of himself in hopes of captivating and influencing whom he believed would become future professionals in medicine, chemistry, pharmacology, and forensic sciences. His philosophical views on drugs, life, sex, personal rights and freedoms, societal concerns, and legal constraints were all freely shared, along with advice to reject out-of-control authority politicizing any area of study, and learning how to ask the right questions. In short, how to perform good science.

Volume One of this three-part lecture series discusses: How a drug gets into the body, how it moves around, what it does, what happens to it, and how it gets out. In doing so, Sasha attempts, as he puts it, to present “what can be bad about drugs, and what is sometimes very good about drugs. Warts and all.”

— Keeper Trout
Author and Editor, *Trout's Notes*
November 2020

LECTURE 1

January 29, 1987

Course Introduction

SASHA: All right. The name of the course is “The Nature of Drugs.” It was originally going to be “Drugs and Society,” which would be kind of a neat thing because you can go and tie everything together in a nice way, but some other department had already stolen the name and refused to give it up. They had to find something new and “Nature of Drugs” had not been used, and so that’s what this will be. But it doesn’t matter very much which name it has or through whose auspices it is authorized, since all of that will have little influence on the content of this course. I intend to cover the area of drugs in the broadest definition of the term, and the attitudes of society towards them.

There are absolutely no requirements for the course. It’s nice if you’ve had chemistry, but I’m going to largely try and resist my big temptation to put great big hexagons on the board with wiggly chains out from the amino groups and methoxy groups and marvelous things like nitrogens. Because this is the heart: I really honestly believe that the knowledge of chemistry is the knowledge of one of the few disciplines that not many people are going to take issue with. You talk about a drug—we’re going to talk about thousands of drugs during the course of the year—and you will often encounter some controversy.

Let’s talk about mescaline, for example. You’ll get controversy as to what it really does, and how it acts, and where it acts in the body, and what these receptor site things are that it acts at, and how it’s metabolized, and whether something is it or not, and is it found in this cactus or that cactus. But you’re not going to take issue that it has this structure.

So, the idea of a chemical structure allows one thing in this very pieced area of so-called science to hang together. You can say what the

compound is, you can say what its structure is, how to make it, and what its properties are, physically, chemically. What it does in the body is into the realms of art. But what it is in a test tube and in a beaker is one of the few really incontestable arguments.

I love chemistry as a focal point from which to say, “Here is a structure. What it does, I don’t know. But maybe it does this and that.” It’s a nice starting spot. I’m going to resist it.

How many people have taken other scientific courses, let’s say botany? Whee! Okay. I’ll introduce some botany. I love it when a few have and most have not because then I can justifiably get into it a little bit further than I normally would.

I was going to introduce myself, but let me introduce you to me first. How many people have taken psychology? Oh, wow! How many people are in psychology as serious business? Well, some of them. At least you’ve gotten into the area.

How many people have taken caffeine? Only two? Oh my, my. I’m in the voting too. I’ve taken caffeine. How many people have taken caffeine? Now that’s more like it. How many people have never touched caffeine? Okay, that’s enough.

By the way, I’m a nut on vocabulary. I love vocabulary and I love using it. Sometimes I get a little bit carried away because I talk about the “hemioptus dysiptria” and I realize that dysiptria is not a common word in everyone’s vocabulary. So, I think if this is going to be the size of the class it’s really going to be neat because then it’s going to be small enough that if someone says, “Hey, hold on. What is dysiptria?” I’ll go into it and we’re off on a tangent.

There’s a textbook for the course. It’s—what is it? *Chocolate to Morphine* by Andrew Weil. It’s a nice one because it honest-to-god presents things as they are. I’m going to have a theme for this whole course called “warts and all.” Namely, what is known about drugs, what is to be found out about them, what do they smell like, what do they taste like, what are the goods, what are the bads. Why is it so bad to use drugs? Why is it occasionally so good to use drugs? It’s going to be an issue of talking

about drugs and their properties. I am not going to champion their use and I am not going to espouse the argument of “just say no.” Nothing along that line has anything to do with drug education. I love the analogy of sex education, which is exactly the same thing if you look at it, just from a different point of view. Sex education: “You’ve got to teach people just to say no.” Well, this is fine and dandy because if they choose to say “yes” then they’re out on their own because they’ve never learned anything outside of the very rudimentary males and females aspect of that.

Let me discover where you are, a little bit. Let me give you three possibilities and have everyone vote on them. The possibilities are: learning at home, learning at school, and learning from your peers. How many learned about sex at home? One, two, three, four, five, six, seven. Okay, that’s about a third. How many people learned about sex at school in some class? Seven. Neat. Eight. How many people learned it from their peers? Eight. Okay, even. Just about even. I trust I shouldn’t have asked how many people know about it. I assume that would have been a universal.

Same argument goes on drugs. You learn an awful lot about drugs from school. But a lot of what you learn is, you know, “Stay away from it.” A lot of people will learn about drugs from home, but not as many as I think should because there is a lot of ignorance at home about what drugs are and what drugs do: “Good god, I smell something strange. You haven’t been—? We gotta go talk to the minister.” This kind of thing is a nice approach to morality, toward ethics, toward what is probably good behavior, and, in many peoples’ eyes is the only right behavior. But it has nothing to do with drug education.

It’s nice to learn it in school, but what you’re going to find are the stereotypes. I saw this very beautifully in medical school where in the second year there was a course called “Pharmacology” that lasted for three quarters. In that class you learned all about pharmacology, which embraces drugs.

One of those three semesters of pharmacology was on CNS drugs: “This will turn ‘em down. This will turn ‘em up. This is a stimulant. This

is a depressant. This is good for treatment of this. And that's good for the treatment of athlete's foot." Then, within that particular semester they had a one-hour lecture that dealt specifically with two topics: one was the psychedelic drugs and the other was smog. And it was all tucked into this short one-hour lecture of which forty minutes was on the psychedelic drugs, and the comments were, "They all cause a toxic psychosis. They are all the same. And substantially the best treatment is Haldol or one of the tricyclic tranquilizers," which are strong or heavy tranquilizers. We'll talk about strong and heavy in a moment.

[Directed to student] Yeah!

STUDENT: When was this?

SASHA: Ah, about fifteen years ago. I don't know if it's changed. I've not been there recently. But this was the attitude that was taken, and you'll still find, "You wanna find out really what is the problem about the use of marijuana? Well, let's go down and talk to our family physician. And he has, by golly, been through those courses and he knows what he's read, that it causes enlarging of this and decreasing of that and maybe increasing of something else." And you ask, "Well, why do people use it?" "Well, there's no really good reason." Nonsense! There's a perfectly good reason. They get high! [Laughter.] And you say, "Well, that's not part of our social ethic. Here, have a cup of coffee and wait until I handle someone else."

We have drugs all through our society. I'm going to start a tally. I wrote notes, shows how much I'm going to use them. We have caffeine. How many people have used alcohol? I'm amongst them. Okay. It's almost embarrassing to ask the question, "Is there anyone who hasn't?" Because the one Mormon, possibly the one Quaker, in the crowd doesn't want to put their hand up. It is all around us. How many people have used tobacco? How many people have not? This is a legitimate question. I have. I can't raise my hand. About two-thirds 'yes,' about one-third 'no.' The fourth I like to put on this list, how many people have used betel nut? One. Any more? Two. I have not. That's one I have not.

STUDENT: What is it?

SASHA: What is it? That's exactly why you're in the course. We're going to find out what it is. These four drugs constitute the four most broadly used psychotropic drugs in the world. Probably, either continuous use or occasional use or association with use of, in the sense of having used yourself, each of these drugs, more than one billion people. In a world of about six billion you're talking about one out of six having used one of these drugs.

Betel nut. We'll probably get to it when we talk about intoxicants and such. It's kind of a nice little thing. It's a little nut about the size of an acorn. It comes out of a palm tree. It's an *Areca*, the genus of the tree. *Areca catechu* is the species name. It's raised from the Philippines westward: the Philippines, the eastern coast of Southern Asia, throughout Southern Asia, into China, across into India and throughout India. It is raised throughout that entire area of the world. It is used by virtually all adults in that world. It is put either dried, different cultures use different ways, but usually it is either dried and used dry and smashed, or it's cut fresh. It's usually taken from the slightly unripe fruit. And it is often, not always, but often, wrapped in a leaf, known as the betel leaf, that comes from a vine belonging to the *Piperaceae* family. That name applies to both the nut from the palm and the leaf from the pepper. It's wrapped in this and shoved into the mouth, up against the gum and the lip. And it's left there. And if you add a little lime to it, make it a little bit basic, it tends to drain out colors and you'll find people often get reddish brown lips and gums and teeth get stained. In fact, black teeth or very dark teeth are a measure, as a beard is in China, of age and wisdom. You've been around a long time, you've used your betel a long time, you've gotten much wisdom from your passage through this vale of tears. And it's not considered a disfigurement, just part of the territory, like wrinkles and emphysema is from smoking. It's all part of the territory and it's a sign of belonging.

You have this as a major, major material. An interesting sideline, I was going to get into this when I got into tobacco and betel, but I'll get into it



now, which shows I'm totally disorganized, but I enjoy doing what I am doing. By the way, thanks for the question. Anytime questions come up, ask them. That's the way I know where you want to go. With betel, you have an alkaloid that's known as arecoline. Maybe I should start writing some of these down. By the way, you'll notice a tremendous resistance to indicate that it happens to be a tetrahydropyridine with a carbomethoxy group on it and an N-methyl.

(This is the sort of thing where I'd love to draw a dirty picture. I call them dirty pictures, things like hexagons with things sticking out and functional groups.)

Arecoline is an alkaloid. How many people know the term "alkaloid?" I'm going to be asking this several times. Not too many. Okay.

An alkaloid is a compound that comes usually out of plants—to a purist it comes out of plants—that contains a basic nitrogen. Usually with some complexity, but not always. It is a base and a caustic material that comes from plants, and most of the active materials, not all, but perhaps nine-tenths of the active materials in human beings that come from plants are alkaloids. Nicotine in tobacco is an alkaloid. Arecoline in the betel nut is an alkaloid. Alcohol is a non-nitrogenous material. Caffeine is a relatively neutral compound that contains nitrogen and is often classified as an alkaloid. Three out of these four major world drug materials are substantially alkaloid containing.

This combination is put together [referring back to betel nut use], it's then put into the mouth, and it's left there. It's always in the same place. It's like a cat chewing on the same tooth. Pretty soon a callus develops there, the tissue becomes hard. The erosion is stopped because of the change in the tissue nature, and it doesn't tend to burn or blister anymore. And when the goodies are depleted, and the person feels the slight euphoria and the fun and the pleasure of it is dropping off, in goes another. And when you go to bed at night, in goes one for the overnight. And in the morning out it comes and in goes a fresh one for the morning. It's like a quid of tobacco; but, this is betel nut. And it has been used

for millennia throughout India, Southeast Asia, into the Philippines, and all through the islands in the Western Pacific.

Now, a problem has come up. This is completely apart from the introduction. A problem has come up in India in the last twenty years. In our culture, there's nothing wrong with shoving a little bit of snuff or a little bit of chopped up tobacco up in there and letting it go. You'll find some people will go through their entire day and night with a tobacco quid.

To touch just a little bit of chemistry, there's a part of the arecoline that is very, very responsive to what are called mercapto groups. In the body, there is a whole inventory of mercapto groups known as—oh, gosh, you have glutathione, you have acetylcysteine. Those in biochemistry could give me a half a dozen more. These little groups are very, very reactive groups.

In tobacco, the principal alkaloid is nicotine. You cure tobacco by putting in nitrites, just like you cure bacon by putting in nitrites. And these nitrites tend to give it an aging, a texture, a smell, a taste that makes your particular tobacco competitive. But this aging takes off the methyl group and puts on a nitroso group on nicotine, so you get what's called in the trade, nitroso nornicotine. This is probably one of the principal agents that is responsible for cancer, and the cancer that comes from tobacco. One whole hour, as you've probably looked ahead, is going to be devoted to tobacco, so I don't want to get too much into this. But this nitroso compound is probably neutralized in the body by these SH [sulfhydryl], these mercaptans, these glutathione and cysteine things. So it takes a long while for the cancer to express itself.

In arecoline, you have something that sops up SH groups and therefore sops up the very thing that makes you protected against tobacco. What has happened in the last twenty years in India is they've begun mixing tobacco and betel together. So you get the euphoria of the betel nut and you get the slight stimulation and the light headedness of the tobacco in the same package, in the same quid. So what's happening in the quid, the component of the betel nut that has the SH group scavenger property robs the body of the defense against the nitroso nicotine

that comes in the tobacco, and in the last ten years the most prominent, the most numerous instances of cancer in India has been cancer of the mouth. It exceeds cancer of the lung, exceeds cancer of the bladder, and other cancers that have been associated with tobacco. Cancer of the mouth, usually of the gum or the throat, or of the jaws, a third level. Adding these two different drugs together for their goodies happens to compensate for the body's own defenses against each of them and here you have a superb example of a social problem—by that I mean preventable cancer—a social problem that comes directly out of drug use that is not only allowed, it's actually encouraged. It's advertised and it's promoted as being a very, very excellent experience.

So, you say, "You should tell them, just say no!" Well, no, you should begin saying there is an interaction here that's got a problem. Be aware of it. This course will be directed towards drug education. Drug education is a search for facts concerning drugs. As I suggested before, the current move to teach people to "just say no" may be good advice for some, and pointless for others, and it has both ethical and moral justification. But it has nothing to do with drug education.

Most of you have already been exposed to drugs, and most of you will personally decide if you wish to become exposed again in the future. The goal of this course is to provide specific information concerning drugs, as to their actions, their risks, and their virtues. And that's really what my role is, I'm a seeker of truth. I'm trying to find out what's there. I am not an advocate for nor an advocate against drug use. I have my own personal philosophies that have no business in here. You'll find that I am quite sympathetic with a lot of drugs that people say are evil and bad. But in truth, I want you to have enough information that you can decide for yourself whether this is something that's your cup of tea, quite literally caffeine, or whether it is something you wish to stay out of.

This is more or less my introduction. I have several bad failings. I jotted some down here to remind myself. One, I tend to lecture a bit too fast. This time I've kept myself under control. You notice we've gone at a very leisurely pace. [Loud laughter.] I'll try to keep it there.