Hallucinogenic Drugs

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Review: Believes that LSD is extremely dangerous, but that it should definitely be available for doctors to study. In general, appears to be torn between telling the truth and believing the evil. If she could get over this, she could be a good writer. She has a hidden sense of humor. See nutmeg, for example.

Foreward

--I. Newton Kugelmass, M.D., Ph.D., Sc.D., Editor

“Dr. Brown of Memphis unravels the dim haze of mystery on the psychoactivity of hallucinogensx 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.”

P. Vi

“Hallucinogens are illegal because of their presumed harmful effects. Unlike opium derivatives, none is addiction; 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."

Chapter I: General Considerations

Names used for hallucinogens: psychotomimetics, psycholytics, psychotogens, phantastica, psychedelic.

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Classification:

1. lysergic acid derivatives

2. indolealkylamines

3. phenylethylamines

4. piperidylbenzilate esters

5. cannabinoids

6. other

Most hallucinogens "identified to date" are alkaloids: having alkaline properties.

"Recent evidence[Schultes, R. E.: Hallucinogens of plant origin. *Science, 163*:245, 1969.] 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 found lysergic acid derivatives in morning glory seeds, Cook and Kieland[Cook, W.B., and Kieland, W.E.: Isolation and partial characterization of a glucoside from *Rivea corymbosa (L.) Hallier Filius. J Org Chem, 27*:1061, 1962.] isolated a glucoside from an extract (ololiuqui) of these seeds which is five times as active as the original extract."

"The terms *addiction* and *habituation* have been almost as controversial as the conditions they describe. Uncertainties over the definitions of these words have plagued scientists, sociologists, legislators, and theologians for years. The term addiction, for instance, acquired a sociological significance with which scientists, particularly, are relctant to deal. Drug *addiction* came to have an evil connotation, more definitive of public mores and attitudes toward a substance than of the capacity of that substance to induce disorders of behavior."

"Tolerance develops with chornic ingestion and modifies drug actions by reducing effectiveness. Most hallucinogens induce tolerance, but not physical dependence."

"Messer [Messer, M.: Running out of an era: Some non-pharmacological notes on the psychedelic revolution. *J Psyched Drugs, II* (Issue I): 157, 1968.] recently added

some new thoughts to an old hypothesis [Sanford, F. H.: Creative health and the principle of "Habeas Mentem." In *Across the Secreatary's Desk. Amer Psychol, 10* (No. 12), 1955.] to explain why men (and women) take drugs. According to him, the present drug problem is a part of the "end of a myth" or the end of a cultural era. The "age of reason and "enlightment" which brought capitalism, music, art, and science, especially science, has become "overripe"; the goals have been achieved. Affluence is an important part of the achievement and is also the shared historical experience of the age group who seek to "cop out." Their subjective experience of the successful economic is that the projbect is completed. They are not concerned with the "struggle for existence" but seek to "pacify existence" or to "indulge in existence." Messer concedes that members of the so-called psychedelic revolution are parasites. However, he exhorts us to accept the historical reality of our position in time; to *live off machine* rather than *like machines*. When the concept of "work" becomes culturally irrelevant, then so will the concept of parasites. Because of their historical location, a considerable portion of today's youth can perceive that we are "running out of era," and they are busing inventing a new myth. The taking of drugs is a part of a serach for a new reality."

Chapter II: Phenylalkylamines: Mescaline and Amphetamines

p. 13-15

"When it is freshly picked, cactus has a water content of 90 to 95 per cent and is difficult to handle, so the ptotoalkaloids, including mescaline, are preferably extracted from the dried cactus. To avoid losses, the plant should be dried at a low temperature as soon as it is collected. Späth and Becke prepared mesaline [sic] as follows:The dried powder from the cactus was extracted with cold alcohol and the latter was removed *in vacuo*. An aqueous solution of the resulting syrup was treated with dilute Hcl and filtered. The filtrate was made alkaline iwth NaOH, and the nonphenolic bases were extracted into ether. After removing the ether, the free bases were distilled *in vacuo*. On treatment with dilute HsSO, mescaline sulfate crystallized. Peyote contains about 6 per cent mescaline."

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"The average dose in man is from 5-7 mg/kg [mescaline] compared to about 1.5 mg/kg for LSD.... Mescaline produces somatic and autonomic effects... such as nausea, tremor, blurred vision, dilated pupils, incoordination, and ataxia. The somatic symptoms which last about one to two hours precede the perceptual and pshycic changes."

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"Mescaline is readily absorbed from the gastrointestinal tract in all species studied, including man."

The biological half-life in cats was estimated 90 to 120 minutes [Neff, N., Rossi, G. V., Chase, F. D., and Rabinowitz, J. L.: Distribution and metabolism of mescaline-^{14}C in the cat brain. *J. Pharmacol Exp Ther, 144*:1, 1964.]

p. 18

"Apparently, the major route of mescaline metabolsim in man is via deamination to yield trimethoxyphenylacetic acid, which is not a psychoactive compound."

"Mescaline has an extraordinary structural resemblance to naturally occurring neuroactive agents such as norepinephrine, and is believed to be derived from dopamine."

P. 19

"Amphetamine (1-phenyl-2-amino propane) was synthesized [Edeleano, L.: Uber einige Derivate der Phenylmethacrylsaure und der Phenylisobuttersaure. *Ber Deutsch Chem Ges, 20*:616, 1887.] in 1887, but its effects on the central nervous system were discovered by [G. A.] Alles in 1927."

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"Over the years, amphetamines have been used by millions as stimulants, and in the control of obesity or other weight problems. Until recently, they were considered to be of such low toxicity that they could be taken without producing toxic manifestations or inducing tolerance or resistence to their action. Considering the large number of individuals who have taken these compounds over long periods of time, the evidence of noxious effects or addiction is rare. Connell has recently shown, hwoever, that following continued usage in some people a condition clinically indestinguishable [sic] from paranoid schizophrenia may occur.... Among other symptoms, there are delusions and hallucinations."

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Included in Axelrod's summary of the effects of amphetamine on catecholamines includes "inhibition of monamine oxidase".

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"Until about 1966, amphetamines were not considered to be a major drug abuse problem. In that year, Griffith and Lemere warned of the extent of danger of abuse, and in 1967 Kalant *et al*. Reported on the effects of intravenous use of amphetamines. Since then there has been an explosive increase in the use of "speed," the street name for metamphetamine [sic].

Prescription daily doses range from 5 mg to "no more than" 20 mg. Intravenous users may inject "from 100 to 1000 mg daily, depending on the degree of tolerance that has been acquired."

"Kramer [Kramer, J. C.: Introduction to amphetamine abuse. *J Psyched Drugs, II* (Issue II):1, 1969.] states that anyone concerned with the welfare of amphetamine users and the users themselves, whould recognize that most, if not all, can recover from even the most profound intellectual disorganization and psychosis, given six months or a year of abstinence."

RELATIVE HALLUCINOGENIC POTENCY OF SUBSTITUTED AMPHETAMINES

Compound	*Ring Position of Substituent*	*Mescaline Units*
Mescaline	3,4,5	1
Trimethoxyamphetamines (TMA)	2,3,4	<2
	3,4,5	2.2
	2,3,5	4
	2,3,6	13
	2,4,6	10
	2,4,5	17
Dimethoxyamphetamines (DMA)	3,4	<1
	2,4	5
	2,5	8
Methylenedioxyamphetamines (MDA)	3-4	3
Methoxymethylenedioxyamphetamines (MMDA)	3,4-5	2.8
	2,4-5	12
	2,3-4	10
Dimethoxymethylenedioxyamphetamines (DMMDA)	2,3-4,5	12
	2,3,4-5	5
Methoxyamphetamines (MA)	4	5
Dimethoxymethylamphetamine (DOM)	2, (4) 5	80
Dimethoxyethylamphetamine (DOET)	2, (4) 5	--

"The cyclic substituent is indcated by a dash between the numbers of the ring carbons involved. Parentheses indicate position of the nonxygen containing substituent. From A. T. Shulgin: Efron, D. H. (Ed.), *Psychotomimetic Drugs*. New York, Raven, 1970.

"The mean effective does [sp] of mescaline was taken to be 3.75 mg/kg. This mescaline unit (M.U.) is subject to much variation and the degree of uncertainty was estimated to be about 25 percent."

On the street, DOM is called STP (serenity, tranquility, peace). At the Haight-Ashbury Medical Clinic, "There were a large number of so-called "bad" trips. At the street level dose (10 mg versus 2 to 3 mg used in the laboratory tests), the peak often lasted from sixteen to twenty-four hours. In some cases, the reaction continued for two to three days."

Chapter III: Lysergic Acid Derivatives

The best known is LSD-25.

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Lysergic acid compounds “are found as natural molecular components of ergot. The latter has had an intriguing history of mixed horror and magic in its own right. [Barger, G.: *Ergot and Ergotism*. London, Gurney and Jackson, 1931.] Ergot is a biological product of a growing fungus, specifically *Claviceps purpura*, which parasitizes cereal grains.... the history and distribution of ergot parallels that of its favorite host, which is rye. Rye was introduced into Southern Europe by the Teutons in the early Christian era. During the Middle Ages, rye bread was eaten largely by the poor, since wheat at that time, because of vicissitudes in agricultural conditions, was regarded as a luxury crop. Rye and ergotism were largely restricted to districts of poor soil and poorer people.”

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“During the middle ages and after, infected rye was used in bread and animal feed and caused major widespread epidemics of ergotism in both people and livestock. Ergot poisoning was of two types, gangrenous and convulsive. The early symptoms of gangrenous ergotism were ingling in the fingers and toes, vomiting, and diarrhea. These were followed by a dry type of gangrene in the extremities, affecting the entire limb which would separate spontaneously at the joint without pain or loss of blood. In convulsvie type, early sumptoms were much the same, but were followed by painful contractions and distortions of limbs, and by convulsions. If the victims survived either type, there were left mentally incompetent.”

Today, Spain and Portugal are “among the world’s major producers” of ergot for “medicinal purposes.”

The basic structural component of ergot is lysergic acid. Various chemical groups can be arranged on this “to give compounds of diverse chemical and physiological properties.”

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Various crystalline ergot products were isolated in 1875 and 1907; Stoll, in 1918, working for Sandoz, realized that these crystalline substances were mixtures and isolated ergotamine. Jacobs and Craig isolated lysergic acid in 1934. Kornfeld, Fornefeld, Kline, Mann, Jones, Woodward “accomplished the total synthesis of lysergic acid in 1954.”

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“LSD remains the King of Psychedelia...”

Original dose of LSD taken by Hofmann was 250 mg which “gave him quite a ride.” Effective oral dose “for the production of psychic phenomena” is .5 to 1.0 mg/kg. Clinical dose “used by some psychotherapists” is 1-2 mg/kg, which is 70-140 mg for a 70 kg person.

Hoffer and Osmond [Hoffer, A., and Osmond, H.: *The Hallucinogens*. New York, Academic Press, 1967.] estimate the LD-50 for man to be about 14 mg.

Intravenous acute LD-50 for mice 46 mg/kg; for rats 16.5 mg/kg; for rabbits .3 mg/kg. For chronic, “rats tolerated 2.5 mg/kg intravenously daily for thirty days. There were no cumulative effects and the animals required the samd Ldj-100 as untreated rats, indicating no development of tolerance.”

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Onset time: orally, 1/2 to 1 1/2 hours. Intramuscularly, about ten minutes; intravenously, a few minutes. “Introspinal injection illicits [sic!] instantaneous effects.”

P. 46

“LSD and other drugs... increase the sort of suggestability which can be produced by the induction of hypnosis.” [Sjoberg, B. M., Jr., and Hollister, L. E.: The effects of psy7chotomimetic drugs on primary suggestibility. *Psychopharmacologia, 8*: 251, 1965.]

“Orally administered LSD is readily absorbed in all species.”

Half-life in man is about 175 minutes, possibly corrected to 109 minutes if it can be “assumed that LSD was equally distributed throughout the tissues”, a possibly precarious assumption.

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Data suggests “that LSD is rapidly disseminated into all tissues, but that it is mainly and rapidly metabolized in the liver, from whence it is secreted into the bile and excreted via the gut. Evidently, the lysergic acid ring is not cleaved or degraded and little destruction of the substituted amide side chain occurs.”

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“Gaddum’s original hypothesis that the psychic effects of LSD are caused by an antagonism of serotonin the the brain analogous to that in muscle was almost immediately discredited. Although 2-Brom-LSD (BOL) is a potent inhibitor of serotonin action *in vitro* and *in vivo*, it is without any effect on the psyche in man.”

“Pretreatment with reserpine enhanced and prolonged the LSD reaction in animals and in man.”

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Cross tolerance occurs between LSD and derivatives such as lysergic acid monethylamide, d-2-brom-lysergic acid diethylamide, psilocybin, mescaline. There is no cross-tolerance to N,N-dimethyltryptamine (whose effects are "similar to LSD") and d-amphetamine (which is chemically related to mescaline).

Nor with D^1-THC (according to Grinspoon, *Marihuana: The Forbidden Medicine*, pp. 2, D^1-THC is another name for D^9-THC).

P. 52

"by 1960 LSD was being considered and seriously tested in the treatment of a variety of mental disorders. Among these were included manic depressive reactions of various types; schizophrenic reactions of paranoid, catatonic and hebephrenic types; involutional psychotic reactions; psychoneurotic reactions of mixed types; alcoholism; chronic psychoses; character and behavior disorders, including homosexuality; pseudoneurotic and borderline schizophrenia. By 1960 LSD had been used in the treatment of practically every type of mental affliction known to man, including drug addiction. Most of the author's [sic] reported efficacy of treatment as either good or promising."

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Studies with control found LSD to be no more effective than a placebo. "Significantly, the latter studies, which incorporated controls as a part of the experimental design, reported *improvement* in *all* categories of subjects; those who received placebo, those who received no drugs, and those who received LSD. However, there was no significant difference between the groups." [However, as I recall, similar studies also showed that therapy itself wasn't any more effective than just hanging loose.]

p. 54

And Dr. Brown knows this, too: "In his discussion of obsolete or outmoded paradigms, Colby states that chaos prevails in psychotherapy; that psychotherapy, as presently defined and practiced, is no science and may never be."

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About Cohen's experiment with 18 LSD users, when he found chromosomal aberations 2-4 times greater than in 14 controls: "Interestingly, this patient group was described as "inveterate experimenters with other drugs" and every subject had taken either one or more of the amphetamines, barbiturates, cocaine, hallucinogens, opiates and phenothiazines. One subject had had phenothiazine at the time blood was drawn. These authors also studied six patients who had not taken LSD, but some other drug, mainly chlorpromazine. Of these, all but one showed an abnormally high incidence of chromosome damage. One detects some lack of candor in describing this study as "chromosome damage incuded by LSD-25." Later studies found no effect of LSD on chromosome changes.

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“These reports, which are apparently published at will in journals with benign editorial review policies, have evoked sensational inferences concerning reproduction and health.”

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Ololiuqui (*Rivea corymbosa*, or morning glory): “Modern Indians grind the seeds, which have a tough outer coat, on a stone, soak them in water or alcoholic drinks, filter them, and drink the filtrate. If the seed coat is not crushed, the intact seed may pass through the gastrointestinal tract without yielding up its magic potent.”

Main component of the ergot indole fraction of *R. Corymbosa* was d-lysergic acid amide (LAA), plus d-lysergic acid methylcarbinolamide (LAM) and “a few minor alkaloids.” This was the first time lysergic acid alkaloids had been found in higher plants. (Previously, only fungi such as *Claviceps*).

Dose: Sixty to one hundred seeds, “ololiuqui produced anergia and irritable apathy, combined with alert thought processes and increased hypnagogic phenomena. Effects appeared rapidly (within 20 minutes), were of short duration, and left no hangover. In doses of 0.5 mg, LAA caused slight nausea, and a tired dreamy, apathetic state. One hour after ingestion, the subject fell into a sleep which lasted for three hours. There were no after effects.”

Types: Heavenly blue (*R. Corymbosa*), Pearly gates (*I. Viol*), or Flying Saucers.

Chapter IV: The Indoles

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Indole-containing compounds comprise about 1/4 of all known alkaloids. However, their chemical structures are highly diverse. “For instance, there is little similarity in the chemical properties of reserpine, LSD, and physostigmine, and even less imilarity in their pharmacological action.”

Three types of hallucinogenic indoles: indolealkylamines (which are potalkaloids); *b*-carbolines (such as harmine) and the iboga alkaloids (such as ibogaine, big surprise).

Indole Alkylamines: Tryptamines

DMT is probably the simplest (N,N-dimethyltryptamine). Is a constituent of snuff from the seeds and pods of *Piptadenia peregrina* and *Piptadenia macrocarpa* Benth, leguminous plants. Cohoba snuff also contains bufotenine (dimethyl-N-oxide, 5-hydroxydimethyltryptamine). It is also in snuff made from *Presotnia amazonica*, although “the validity of this observation has been vigorously contested on the grounds that the source material was probably *B. Rusbyana*...” DMT occurs in *Lespedeza bicolor japonica*, and the root of *Mimosa hostilis* Benth.

P. 80

“Bufotenine was first isolated [Bertrand, G., and Phisalix, C.: Toxicité comparée du sang et du venin de crapaud commun (Bufo vulg.), considérée au point de vue de la sécértion interne des glandes cutanées de cet animal. *Compt Rend Acad des Science, 116*:1080, 1893.] from the secretions of the toad, *Bufo vulgaris* in 1893... [and] is present in significant proportions in practically all of the various plants form which hallucinogenic snuffs are made.... However, snuff made from these materials also contain DMT and 5-methoxydimethyltryptamine in about the same amounts. There has been some controversy as to whether bufotenine has any hallucinogenic activity.... This compound has extremely painful and dangerous cardiovascular effects and cannot be used without caution in man. It would be difficult to differentiate whether a psychotic reaction were due to central effects or cardiovascular action.”

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Phalaris tuberosa L. and *P. Arundinacea L.* are grasses that contain 5-methoxyN-methyltryptamine, and cause “staggers” in animals. *P peregrina* bark contains that and also 5-methoxy-N,N-dimethyltryptamine.

Psilocybin:

“Spanish historians who wrote about peyote and ololiuqui also described the “sacred mushroom,” teonanacatl. The intoxicating mushrooms were eaten by the Indians at feasts and religious ceremonies, and by special classes of folk, such as witch doctors and soothsayers. Imbibers were subsequently endowed with clairvoyance and divine powers....

‘The use of mushrooms in Mexico and Central America for social and religious purposes had apparently disappeared except for a few isolated Indian tribes in remote mountainous districts of Mexico. Stimulated by reports that mushrooms were still being eaten for purposes of magic in southern Mexico, the Wassons made several trips into these regions in search of the culture and the mushrooms. In 1955, Gordon Wasson actively participated in an Indian mushroom ceremony in Huautla de Jimenez, Oaxaca.... They were of the family Strophariaceae and mostly of the genus *Psilocybe*.... The main active component, 4-phosphoryloxy-N,N-dimethyltryptamine, was named psilocybin, and an accompanying compound, present in much smaller amounts, was called psilocin. The latter was later found to be 4-hydroxyl-N,N-dimethyltryptamine, ahydrolysis product of pilocybin.”

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“Psilocybin and psilocin produce hallucinogenic effects which are entirely analogous to those produced by LSD and mescaline, but the frequency and intensity of the effects vary with the dose. The dose required to elicit LSD-like symptoms is from 4 to 8 mg. However, a dose of from 115 to 160 *m*g per kg orally is sufficient to elicit a minimum response. The threshold dose is about 60 *m*g per kg. The syndrome pattern becomes apparent within thirty minutes of an oral effective dose; parenterally, these symptoms appear within five minutes of injection. Doses of 6 to 20 mg cause much more profound psychic changes than the lower amounts and lead to illusions and hallucinations. The hallucinogenic properties of psilocybin, psilocin, LSD and

mescaline are essentially identical, except that the time course for the tryptamines is shorter."

"Some of the autonomic effects are dilation of the pupil, piloerection [get yer mind out of the gutter! That's *raising hair*], temperature increase, etc. The pharmacologic effects of psilocin and psilocybin are practically identical. Thus, the phosphoric acid radical appears to contribute little or nothing to the pharmacological efficacy of psilocybin. Since dephosphorylation is readily accomplished by alkaline phosphatase, it has been suggested that psilocin is the active component *in vivo*. The administration of psilocybin to mice results in an accumulation of psilocin in the kidney, liver and brain.... Behavioral effects closely followed the increase in brain levels of psilocin and there is evidence that the CNS effects are exerted only after psilocybin is converted to psilocin."

P. 86

"The toxicity of psilocybin is low. In mice, it is 2.5 times less toxic than mescaline, while it is fifty times more effective as a hallucinogen in man. [Hofmann, A.: Psychotomimetic agents. In Burger, A. (Ed.): *Drugs Affecting the Central Nervous System, Medicinal Research Series 2*. New York, Dekker, 1968, p. 169.]

"it is interesting to note that heart and kidney contain an oxidase which transforms psilocin into a blue-colored quinone-like compound."

b-Carbolines:

"The *b*-carbolines are a group of heterocyclic indole compounds among which are included the harmala alkaloids. Hallucinogenic compounds of this type have been identified as the active ingredients of a group of bizarre "magic drinks" prepared from the Malpighiaceae family of plants. The most widely used species are from the genus, *Banisteriopsis*. From *Banisteriopsis caapi, B. Inebrians,* and *B. Rusbyana*, Indian tribes in parts of Brazil, Bolivia, Colombia, Ecuador, Peru and Venezuela make hallucinogenic extract which has been given a variety of names. A related genus *Tetrapteris methystica* has also been used for this purpose. Although the magic potion is called by many vernacular names, ayahuasca, caapi, natema, pinde, and yajé, among others, the active ingredients are the same. For the most part the same, or closely related, plant is used in making the decoction. Usually only one type of plant is used, but in some areas of the Amazon the preparation may include the bark of *B. Caapi* and the leaves of *B. Rusbyana*. Sometimes plants which have toxic properties are added--*Alternanthera, Psychotria, Nicotiana,* and *Datura*. The active ingredients of the latter are atropine and scopolamine."

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"In large doses harmine causes tremors, reminiscent of some of the indole alkylamines, and clonic convulsions. With toxic doses, respiratory arrest occurs, and there is a fall in temperature. The drug causes a weakening of cardiac muscles which results in a vasodepressant effect. Partial reduction of harmine leads to a greater toxicity since harmaline is about twice as toxic to experimental animals as is

harmine.... The effects of harmine and derivatives in animals, particularly the excitant effects, are related to their capacity to inhibit monoamine oxidase."

"recent studies confirm that harmaline is hallucinogenic in doses of 1 mg per kg intravenously, or 4 mg per kg orally. In humans, subjective effects occur with doses of 35-45 mg of harmine injected intravenously. The material is rapidly lost from the blood, suggesting rapid distribution to the tissues."

P. 92

"Some of the responses to harmaline are nausea, dizziness, and general malaise; parasthesias of the hands, feet, and face occurs, followed by numbness. Distortions of body image and of objects in the environment, so frequent with LSD and mescaline, are not present. The same is true in regard to color enhancement."

Iboga Alkaloids:

"Alkaloids obtained from the root bark of the African shrub, *Tabernanthe iboga* are another series of indole-containing compounds which are of possible interest in the study of hallucinogenic drugs. The natives of West Africa, especially of Gabon, chew the root of *T. Iboga* to offset hunger and fatigue.[Tyler, V.E.: The physiological properties and chemical constituents of some habit-forming plants. *Lloydia, 29*:275, 1966.] Extracts of the plant are said to be used by natives while stalking game to enable them to endure motionless periods for as long as two days while remaining mentally alert[Stecher, P. G., Finkel, M. J., Siegmund, O. H., and Szafranski, B. B. (Eds.): *The Merck Index of Chemicals and Drugs*, 7th ed. Rahway, N.J., 1960, p. 549.]. In large doses, iboga causes excitement, mental confusion, and a drunken madness characterized by prophetic utterances. The principle alkaloid of at least twelve which can be isolated from these extracts is ibogaine."

Chapter V: Marihuana

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"Marihuana is a name for one of the several types and kinds of hallucinogenic preparations which can be obtained from *Cannabis sativa* L. (family Moraceae). The name of the preparation depends upon the part of the world in which the plant is grown, as well as from what part of the plant the preparation is made. The potency however, depends on the genotype rather than the soil and climate as was previously thought. [Quimby, M. W., and Doorenbos, N. J.: School of Pharmacy, University of Mississippi, University, Mississippi, 1969.]"

There are separate male and female plants (dioecious). Two varieties: *indica* and *non-indica*. It is an annual "and will grow almost anywhere." "The flowering top and adjacent leaves (bracts) of the plant are covered with glandular hairs which secrete a sticky resin. Formation of the latter ceases when the seeds mature, and it has been proposed that the function is to protect them during the ripening season." "In the United States, marihuana may be called "weed," "stuff," "Indian hay," "grass," "pot," "maryjane," "tea" and God only knows what else."

An “excellent” historical summary of marihuana: Walton, R. P.: *Marihuana*. New York, Lippencott, 1938, p. 167.

The activities (after 1840) of O’Shaugnessy, Aubert-Roche, and Moreau de Tours “resulted in widespread and general use of the drug in Europe and in America. This popularity can be attributed partly to the fact that the drugs were introduced prior to the appearance of synthetic hypnotics and analgesics. At that time, the only drug commonly used for these purposes was morphine. Hemp drugs do not exhibit certain of the notorious disadvantages of the opiates. They do not constipate, they increase rather than decrease appetite, they do not depress the respiratory system even in high doses, and the liability of developing addiction is not great.”

P. 104

“Much has been written, but little has been told about marihuana.”

P. 106

“Psychotomimetic effects” produced by “about” 200 *m*g/kg smoking, 480 *m*g/kg orally.

P. 108

“In a neutral setting, the physiological and psychological effects of smoking marihuana appeared to reach a maximum intensity within thirty minutes and to be completely dissipated after three hours.”

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There are four methods of numbering the cannabinoid structure: pyran, dibenzopyran, biphenyl, and terpine [monoterpene?]. Depending on which system is used, THC may be called D^1-THC or D^9-THC.

It is not an alkaloid.

P. 115

“For almost every neutral constituent, hashish contains an analogous acid. The cannabinoid acids are not hallucinogenic. When they are heated, they are rapidly converted into the respective neutral compound. As mentioned earlier, this may well be one of the reasons why marihuana has a higher activity if it is smoked than if ingested.”

Cannabidiolic acid is the predominant one.

Chapter VI: Piperidyl Benzilate Esters and Related Compounds

The Solanaceae is "one of the richest alkaloidal plant families," encompassing the potato, eggplant, belladonna, and deadly nightshade. Some, such as the genus *Datura* "have been recognized as poisons and narcotics since antiquity, and some have been used in religious and magic rites. [Schultes, R. E.: Hallucinogens of plant origin. *Science, 163*: 245, 1969.]"

p. 123

"An interesting use is made by the Jivaro tribes. Unmanageable children are given *Datura* seeds in the hope that the spirit of their forefathers may come to admonish them." [No cite.]

p. 124

"Most, if not all species of *Datura* of North America, Europe and Asia, as well as the tree species of South America, contain similar tropane alkaloids such as hyoscyamine and its racemic isomers, atropine, and scopolamine."

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"Hofmann [Hofmann, A.: Psychotomimetic agents. In Burger, A. (Ed.): *Drugs Affecting the Central Nervous System. Medicinal Res Series.* New York, Dekker, 1968, vol. 2, p. 169.] rejects them as specific hallucinogens, and relegates their psychotomimetic properties to side effects or toxicity."

"Thought processes are severely disrupted. Speech is disorganized and incoherent; confusion, disorientation, and amnesia occur often and may be long lasting. These symptoms wax and wane, typical of a true delirium. The amnesia is striking, particularly following doses great enough to produce delirium. At lower doses, memory may not be significantly affected, but the ability to concentrate may be altered. A subject may start to answer a question, but change to a completely irrelevant thought in midsentence. He may then suddenly become aware of an inability to control or concentrate thought, and become bewildered, often returning to the original topic or asking that a question be repeated."

"At the upper dose range, mental disturbance may last for twenty-four hours with some confusion remaining for days."

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"Sernyl is the trade name (Parke Davis and Co) for 1-(1-phenylcyclohexyl) piperidine". Dosage ranges from 0.05 to 0.2 mg/kg. "Intravenously, striking effects may be obtained in minutes; intramuscularly, the effects are less marked, but may be prolonged. [Hello? Could this mean Ketamine and PCP are even closer than even *I've* argued?]

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“A recent symposium began with a lengthy discussion of the problems of defining drug states in terms of schizophrenia. The discussion ended with a conclusion that the use of drugs as models for schizophrenia, or vice versa, is premature in light of the fact that we don’t know what schizophrenia is.”

Chapter VII: Some Minor Hallucinogens

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Fly agaric: “According to Wasson, the effects of ingesting fly amanita are apparent within fifteen to twenty minutes, but may last for hours. The first reaction is soporific--the recipient falls into an abnormal sleep, marked by colored visions. After waking from this sleep, some subjects express feelings of elation that lasts for three or four hours. During this state, the subject is often capable of extraordinary physical feats and enjoys performing them. One of the most extraordinary features of fly agaric is that the hallucinogenic properties pass into the urine. Thus, one may enjoy the euphoriant over and over again or pass it among friends (or enemies)! Obviously, the active ingredient is ingested and excreted unchanged. Or, an inactive constituent may be activated by metabolic processes *in vivo*.”

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Muscarine is present, but “not considered to be the centrally active constituent.” Muscimole and ibotenic acid have been isolated. Muscimole “is very polar and extremely water soluble.” Ibotenic acid is an amino acid, “present to the extent of 0.3-1.0 gm per kg.”

Ultraviolet irradiation *in the laboratory* of ibotenic acid gives muscazone, “which is pharmacologically less active.”

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Sedative action obtained with 4-8 mg ibotenic acid/kg, and 1-2 mg muscimole per kg injected intraperitoneally. Oral administration about one-half as effective.

Nutmeg comes from the nutmeg tree, *Myristica fragrans*. A tropical plant, it grows “particularly well” in the East Indies and Caribbean. It is dioecious, with male and female flowers. Nutmeg is from the seeds. Mace is from the “aril, a bright red covering which can be peeled away from the seedcoat.”

M. Fragrans was unknown in Europe until the time of Marco Polo, when the Portuguese controlled the nutmeg/mace trade. When the East Indies came under the control of the Dutch, the Dutch limited nutmeg cultivation to increase the price of it, but French and British traders managed to break the monopoly, and cultivation spread throughout the tropics.

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“The use of nutmeg as a medicant was first recorded by the Arabs about 600 A.D. It was used for kidney disease, pain and other ailments, particularly digestive disorders. Inevitably, it was described as an aphrodisiac; in some Arabian countries men still take it to increase virility.

‘In Hindu medicine, nutmeg was used for fevers, respiratory dysfunction and heart disease. It is still used as an analgesic and sedative by folk doctors and is given in small doses to quell hysterical or unmanageable children, the number of which seems to always increase in direct proportion to increased virility.”

“near the turn of the 20th Century, a mistaken belief that nutmeg would induce abortion and bring on overdue menses caused many incidences of nutmeg poisoning. A summary of symptoms described in these cases were restlessness, dizziness, fear of death, coldness of extremities, nausea, vomiting, and abdominal pain. Patients were likely to be extremely agitated and delirious with weak rapid pulses and decreased body temperatures. These symptoms resulted from the oral ingestion of one to three nutmegs.”

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The hangover for nutmeg: “a blooming headache, dry mouth, tachycardia, dizziness and general malaise”.

Psychological reactions: not likely with small doses. With higher doses it may range from nothing to hallucinogenic experiences analogous to those caused by LSD or mescaline. “There is no direct correlation between dose and psychoactivity”, probably due to differences in potency or in sensitivity of the recipient.

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Kava is a Polynesian beverage, “prepared by steeping the pulverized roots of the Kawa, or Kava-Kava plant (*Piper methysticum* Forster) in water until a cloudy, khaki-colored liquid is produced. In times past, the extraction was preceded by a mastication step, that is, the roots were chewed for a time by selected members of the group, usually young boys, before the water was added.”