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LSD 1848/PSI/OL

Psychotomimetics and Their Abuse*

Dr. Ara Der Marderosian

"You would not find out the boundaries of the psyche, even by traveling along every path; so deep is its measure and meaning." (Heraclitus)

Man has long known from primitive times how to use various substances in his environment as drugs. They have served many medical, social, magical, and religious purposes. Those who were versed in the knowledge, preparation, and administration of these products and an interpretation of their effects were highly respected and regarded by their followers. We find also that the ancients stood in awe of the powerful mind-altering agents and truly believed that God revealed himself in their own bodies through them. Hence they were used mainly to promote certain social goals, further their cultures and enhance their religious beliefs. Though based largely on fear and ignorance, their taboos and folk wisdom guarded fairly well against excesses in abuses.

Such is not the case today in our so-called sophisticated and highly advanced society. Although many do respect and understand the value and proper use of drugs against the ills of mankind, a large segment of our society today apparently does not share this philosophy. They seem intent on

playing, "chemical Russian roulette" and further, subverting the potent effects of the mind-altering agents to enhance their purported, "new," "instant," "easily available," "profound," pathways to hedonism, introspection, passivity, mysticism, and nihilism. It is the purpose of this discussion to focus on this abuse and consider the current status of the psychotomimetic or hallucinogenic drug misuse.

As early as the late 1800's, Louis Lewin, one of the most prominent pioneers in psychopharmacology, brought attention to the psychotropic or mind affecting drugs (1). It was his early work which later laid the groundwork for the current classification of the psychotropics into the calmatives or tranquilizers such as chlorpromazine, the hypnotics such as the barbiturates, the stimulants such as the amphetamines, the antidepressants such as the monoamine oxidase inhibitors, the analgesics and euphoricants such as opium and its derivatives, the intoxicants or inebriants such as alcohol and ether, and the psychotomimetics or hallucinogens such as LSD (D-lysergic acid diethylamide) and mescaline.

Lewin used the word "phantastica" to describe those drugs which give rise to sense illusion. It probably is a better word than the commonly used terms "hallucinogen" or "psychotomimetic" because true hallucinations do not always occur and the psychotic

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state is not truly mimicked. Other terms, equally lacking in their ability to successfully describe the effects of these drugs, include psychotogenic, euphorgenic, schizogenic, psychotica, psycholytic, psychodysleptic, and psychedelic. Each has its own shade of meaning depending on who originally presented them for use and the whim of those using the terms. All agree, however, that these agents elicit profound psychic phenomena which deal with alterations in perception and reality of space and time.

The interpretation of these effects and their meaning is the major point of contention between those who believe that the hallucinogens should be used for social, philosophical, and religious reasons and those who believe that the hallucinogens should *not* be used because of their potential deleterious effects on the mind. The other psychotropics exert influence mainly on mood, and depression or stimulation of consciousness.

History and Botany

The plant kingdom has and continues to be our chief source of the necessities of life. The process of photosynthesis provides not only oxygen and the plants themselves as sources of food, clothing and shelter, but also many of the important drugs used in medicine like *Digitalis*, reserpine, and precursors for most of our steroids. Many of the synthetic drugs are, in fact, based on molecules originally elaborated by nature. Yet only about 3 percent of the plants have been chemically and pharmacologically evaluated as sources of drugs. In fact, of the more than 800,000 or so species of plants, only some 3000 species serve directly as food and, of these, about 150 angiosperm species are considered of sufficient importance to enter the world's commerce. Only 12 to 13 cultivated species stand be-

tween the world's population and starvation (2-4).

An analogous situation exists with the plants used as narcotics.* Of the 60 odd species thus far uncovered as being employed in primitive cultures as intoxicants, about 20 are of major significance. Even fewer; e.g., some of the hallucinogenic mushrooms, peyote cactus, certain morning glory seeds, and marihuana, enjoy widespread use. However, as legislation has restricted the availability of LSD and some of the other synthetics—so will the use of some of the readily available euphorgenic botanicals rise. In Table I, we see listed some of the more prominent members in eight botanical families and their contained active principles.

A thorough consideration of the historical use of all of the botanical sources of narcotics is beyond the scope of this discussion. Suffice to say that they have played and continue to play major roles in many primitive societies, particularly in the New World; viz., parts of Mexico and South America, and as far north as the midwest part of the United States and extending up into Saskatchewan in Canada.

The "Teonanacatl" or "flesh-of-God" sacred mushrooms (*Psilocybe* spp.) played an important role in pre-Columbian cultures of Central America and are still used in some of these remote regions in religious ceremonies (5). So also with the peyote cactus or *Lophophora williamsii*, known by its Aztec name, "peyotl." In the 19th century, the peyote cult spread north to the American Indians where it evolved into the central religious drug of the Christian institution, the Native American Church. Protected by the religious freedom guaranteed by our constitution, this rite is still extant in many parts of the midwest (6).

* Used here in the classic sense meaning "to benumb."

Source and

Moraceae:

Cannabis

Cactaceae:

Lophophora
or *Anhal*

Leguminosae:

Piptadenia
Piptadenia

Malpighiaceae:

Banisteria
Tetrapleura

Piperaceae:

Piper

Rutaceae:

Peganum

Agaricaceae:

Psilocybe
Stropharia
Conocybe
Amanita
agaric)

Convolvulaceae:

Rivea coccinea
(ololiuqui)

Synthetic:

The "ololiuqui"
(*Rivea coccinea*) now
Aztec origin
in religious
motive motif
(7).

Hashish
resinous
or marihuana

Table I

Botanical Sources of Psychotomimetic Substances (11)

Source and Common or Native Name	Active Principles
Moraceae:	
<i>Cannabis sativa</i> L. (hashish)	tetrahydrocannabinols, etc.
Cactaceae:	
<i>Lophophora williamsii</i> (Lem.) Coulter or <i>Anhalonium lewinii</i> Lem. (peyote)	mescaline (active dose: 0.3-0.5 Gm.)
Leguminosae:	
<i>Piptadenia peregrina</i> Benth. (cohaba) <i>Piptadenia macrocarpa</i> Benth.	N,N-dimethyltryptamine, bufotenin (active dose: 0.05-0.07 Gm.)
Malpighiaceae:	
<i>Banisteriopsis</i> spp. (caapi) <i>Tetrapteryx</i> spp. (yage, ayahuasca)	harmine, harmaline (active dose: 0.1-0.4 Gm.)
Piperaceae:	
<i>Piper methysticum</i> L. (kava kava)	unknown
Rutaceae:	
<i>Peganum harmala</i> L.	harmine, harmaline
Agaricaceae:	
<i>Psilocybe</i> spp. (teonanacatl) <i>Stropharia cubensis</i> Earle <i>Conocybe</i> spp. <i>Amanita muscaria</i> (Fr.) Quel. (Fly agaric)	psilocybin, psilocin (active dose: 0.006-0.015 Gm.) active principles unknown
Convolvulaceae:	
<i>Rivea corymbosa</i> (L.) Hallier f. (ololiuqui)	d-lysergic acid amide, d-isolysergic acid amide, elymoclavine and re- lated compounds (active dose: 0.001- 0.002 Gm.)
Synthetic: LSD	d-lysergic acid diethylamide (LSD- 25) (active dose: 0.00002-0.00006 Gm.)

The "ololiuqui" and "badoh negro" (*Rivea corymbosa* and *Ipomoea violacea*) morning glory seeds are also of Aztec origin and their use continues in religious and divinatory rites in remote mountain areas of South Mexico (7).

Hashish, the concentrated euphoric resinous principles of *Cannabis sativa* or marihuana, has been known as an

intoxicant in the near and far East for thousands of years. It is described in the early medical and mystical writings of the Chinese and Indians and is still socially acceptable and widely used in parts of these countries (8, 9).

In the Western Amazonian regions, the natives consume a narcotic drink known as "ayahuasca" (Ecuador, Peru,

Bolivia), "caapi" (Brazil and Colombia), and "yage" (Colombia) which is prepared from the malpighiaceae vines of various species of *Banisteriopsis* and *Tetrapteryx*. This, too, is consumed for prophetic and divinatory purposes (5).

Various snuffs which are administered by blowing into the nose are prepared from leguminous *Piptadenia* spp. and myristicaceous *Virola* spp. The former, known as "cohaba" is used by South American Indian tribes in the Orinoco region to conjure visions and render warriors fearless and insensitive to pain. The latter, known as "Yakee" or "Parica" snuff is used also for its hallucinatory effects (5).

Thus we see that the literature is replete with many examples of botanicals used as mind-altering agents. Their migration into the United States is an interesting contemporary historical development being currently

fostered by the widespread search for less potent and less dangerous substitutes for LSD. The enormous increase in illegal importation of marihuana, the use of locally grown morning glory seeds, the ingestion of large doses of nutmeg which is related to *Virola* mentioned above, and even attempts to bring the hallucinatory mushrooms into this country are a few examples (7, 10).

Chemistry

In order to fully comprehend the relationships which exist between the active principles reference is given to Figure 1 which shows how most of these compounds are in reality indole type or tryptamine based compounds with certain variations.

The indole nucleus is shown in the center of the diagram. At the top, one can see how orientation of the ethylamine side chain "downward"

can yield a small amount of indole nucleoside. Mescaline from the fact been prepared *in vivo* to this is felt to be (11). The mescaline is a catecholamine epinephrine from the str

On the left side of the chart in the "upper" part, the close structural relationship between serotonin or 5-HT and the important humoral factors and the effects of the various derivatives of ergot alkaloids (*purea*). Later, certain lysine-related compounds and certain specific

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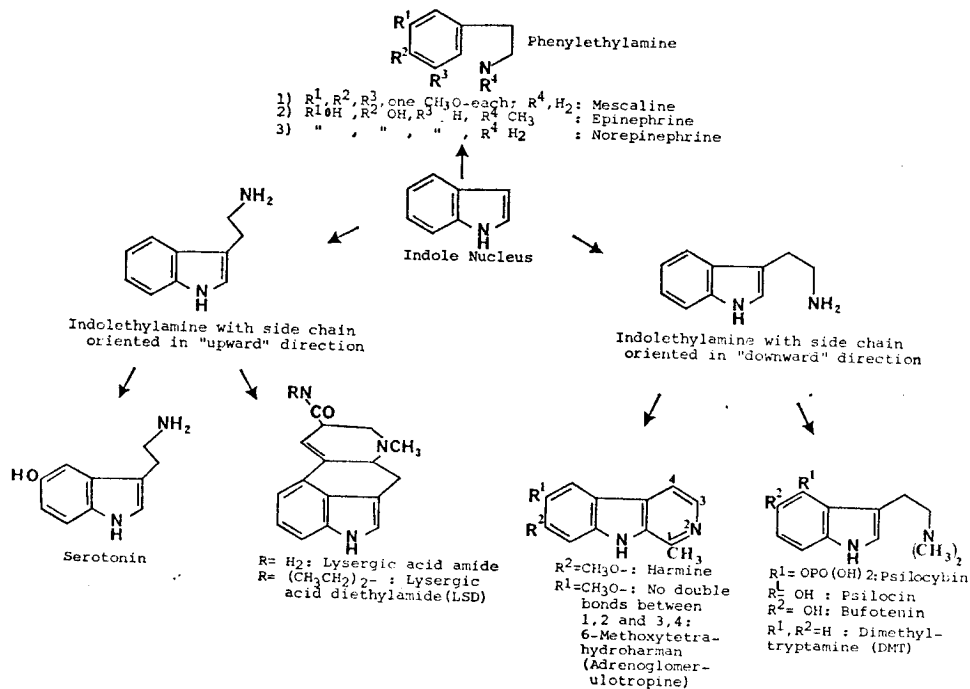


FIG. 1—STRUCTURAL RELATIONSHIPS BETWEEN PSYCHOTOMIMETIC SUBSTANCES.

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comprehend the exist between the prence is given to ws how most of in reality indole ased compounds ns. s is shown in the m. At the top, icentiation of the in "downward"

can yield a structure quite close to the indole nucleus. The compound, mes- caline from the peyote cactus, has in fact been proposed to be transformed *in vivo* to an indole derivative and this is felt to be the active species (6, 11). The close relationship between mescaline and the two endogenous catecholamines, epinephrine and nor- epinephrine is also quite apparent from the structures given.

On the left of the figure, orienting the side chain of the indoethylamine in the "upward" direction, gives us the close structural relationships obvi- ous between LSD and serotonin. Sero- tonin or 5-hydroxytryptamine is an important normal endogenous neuro- humoral factor. The hallucinatory effects of the compound LSD were accidentally discovered in 1943 by Hofmann (11, 12) during synthesis of derivatives from principles isolated from ergot fungus (*Claviceps pur- purea*). Later work (7) showed that certain lysergic acid amides and re- lated compounds were also present in certain species of morning glories.

On the right of Figure 1, it can be seen that orienting the side chain of the indoethylamine in the "down-

ward" direction gives the close struc- tural relationships obvious between the harmine indole alkaloids of *Ban- isteriopsis* spp. and the psilocybin in- dole alkaloids of the Mexican hallu- cinatory mushrooms (*Psilocybe* spp.). In addition, one can see the close structural relationships between others including DMT (N,N-dimethyltrypta- mine) and adrenoglomerulotropine (6-methoxytetrahydroharman). This latter compound is a pineal gland metabolite and has been claimed to be the first naturally occurring en- dogenous psychotomimetic (13). It is, coincidentally, an isomer of tetrahy- droharman, one of the hallucinogenic indole alkaloids of *Banisteriopsis* spp.

It has been proposed (14) that those structures which are capable of form- ing rings analogous to the B or C ring in LSD have hallucinogenic potential. In Figure 2, a few structurally possible rearrangements of psilocin, and one of the amphetamines, TMA-2 (2,4,5- trimethoxyamphetamine) in confor- mation with the B and C rings of LSD bear this out. Not only does this pro- posal help explain why certain of the amphetamines show psychotomimetic activity, but it may be the "missing

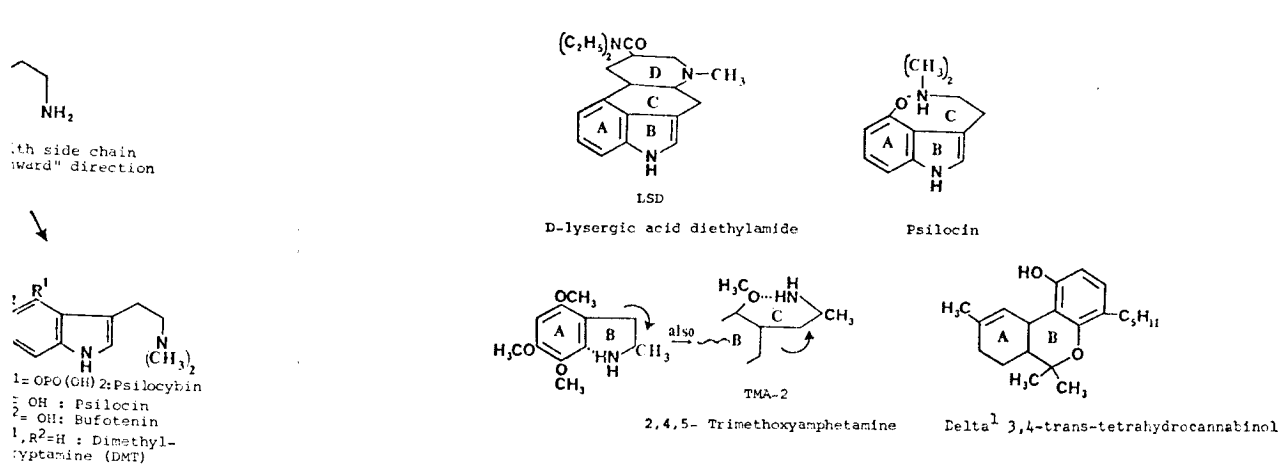


FIG. 2—STRUCTURES HAVING HALLUCINOGENIC POTENTIAL.

SUBSTANCES.

link" in explaining the action of the tetrahydrocannabinols, the only nitrogen free nonindole euphorogens, and the active principles of the resins of marihuana. The atomic radii of nitrogen (indole nucleus) and oxygen (tetrahydrocannabinol nucleus) are quite close which means they are similar in size and may help these structures fit the same theoretical receptor site inferred in these proposed structure-activity relationships.

Much has been said about the ease of synthesis of the various psychotomimetics ranging from statements that a high school chemistry student could make them to statements that only qualified competent chemists possess the knowledge needed to prepare them. The answer lies somewhere in between. Given the proper starting materials (e.g., lysergic acid and diethylamine) and directions, it may be relatively simple. However, it is in the final purification steps that difficulties lie. Not properly carried out, they lead to impure mixtures which enter the black market and increase the toxicological dangers of the compounds.

Many of the 45 or so clandestine laboratories raided in the past 18 months by agents indicate that there is a flourishing underground press which makes available "recipes" for these substances. The irresponsible chemistry major college dropouts and their cohorts have obtained certain patents or raided the legitimate scientific literature and have developed capabilities of preparing a wide variety of psychedelics, including LSD, mescaline, psilocybin, and a number of hallucinogenic amphetamines. This, either for personal financial gain or status or to further their belief that they are the self-appointed chosen apostles for sustaining the "tune-in, turn-on, drop-out" psychedelic movement.

Their cleverness is indicated in their ability to add extraneous material to the active substances in order to "cover them up." These serve to confound forensic analyses of confiscated samples. Recent reports on the isolation, identification and synthesis of the active principles of marihuana (delta¹ and/or delta⁶ 3,4-trans-tetrahydrocannabinol) forewarn of its appearance on the blackmarket in the near future (14).

There remains another recent area of abuse of drugs; namely, those agents originally intended for use as anti-asthmatics (15, 16). They include certain powders and cigarettes formulated using the leaves of *Datura stramonium* and *Atropa belladonna*. Both plants contain the parasympatholytic belladonna alkaloids and have aboriginal historic use as intoxicants in the American Southwest (New Mexico, California, Arizona, and Mexico). These have long use in medicine in this country and, on inhalation of smoke from the burning leaves mentioned above, sufficient quantities of atropine and congeners contained therein are absorbed. These effect paralysis of the endings of the pulmonary branch of the vagus which relieves the bronchial spasm. Although of little use today because the temporary relief thus obtained may be followed by exacerbation of the condition due to bronchial irritation, these products have found their way into the "thrill-seekers" market.

Consumption of large quantities (several teaspoonful amounts) in various beverages leads to the classic intoxication by the belladonna alkaloids often accompanied by bizarre hallucinatory effects. In fact, the atropine molecule has served as a prototype for the preparation of a series of synthetic compounds capable of producing auditory and visual hallucinations, disorientation, mood changes, and para-

noid and humans (1) and glycol structural tropane molecule are c Figure 3.

Pharmacology

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noid and hypochondrical delusions in humans (17). The piperidyl benzilate and glycollate derivatives which show structural resemblance to the basic tropane nucleus of the atropine molecule are examples and are shown in Figure 3.

Pharmacology

Reference to Table II leads us to certain important pharmacological considerations. For the most part, it may be observed that the majority of the popular psychotomimetics are effective by the oral route of administration. Only marihuana, which is commonly smoked and DMT, which is injected, snuffed or smoked, are exceptions.

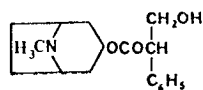
Dosages range from microgram quantities as with the most potent hallucinogen, LSD, to larger gram quantities of crude plant material as with marihuana and peyote cactus. Duration of action varies with dosage and character of active principle, again with LSD at the top and marihuana and cactus "buttons" (transverse slices of the crown of the cactus) at the bottom of the potency scale.

The actual pharmacological effects also vary considerably. For the most part, the psychotomimetics influence both the peripheral autonomic nervous system and the central nervous

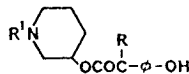
system. Some of the adrenergic effects seen in the former include slight dilation of the pupils (mydriasis), slight increase in heart rate (tachycardia) by 10 to 20 beats per minute, and a slight rise in systolic and diastolic arterial pressure of from 10 to 20 m.m. Hg. Concomitant rise in blood glucose levels of from 10 percent to 20 percent may also be observed in addition to increased spinal reflexes.

All of the autonomic effects, however, are dwarfed by the enormous psychic effects. There is distortion of sense perception which accounts for the visions, pseudo-and true hallucinations, dreamlike thoughts, dream images, and depersonalization. Accompanying this are a wide range of emotional reactions which depend largely on dosage, inherent suggestibility and personality of the subject, and the surroundings in which the psychotomimetic is administered (11, 12, 18-20). These last few considerations affect whether a "heavenly" or "hellish" response is elicited. Some of the hallucinogens appear to precipitate reappearance of the effects weeks or even months after use of the drug ceases.

Such phenomena as "religious" or "consciousness-expansion" effects are highly personal interpretations of the meanings of these hallucinations.



Atropine
(dl-Hyoscamine)



- (1) 1-Methyl-3-piperidyl benzilate (R=phenyl; R¹=CH₃)
- (2) 1-ethyl-3-piperidyl cyclopentylphenylglycollate ("Ditran") (R= cyclopentyl; R¹= ethyl)

FIG. 3—STRUCTURAL RELATIONSHIPS BETWEEN ATROPINE AND A FEW SYNTHETIC HALLUCINOGENS.

Table II

Name	Origin	Mode of Administration	Dosage	Duration of action	Pharmacological effects	Dangers inherent in use
Marihuana (Pot. grass, hashish, reefers)	<i>Cannabis sativa</i>	Smoked, swallowed	1-5 cigarettes, or several grams ingested	4-6 hours	Relaxation, euphoria, hallucinations	Perception and judgment alteration
d-lysergic acid diethylamide (LSD, acid, sugar)	<i>Claviceps purpurea</i> and synthetically	Oral ingestion	100 micrograms	10-12 hours	Excitation, intense visual & auditory hallucinations, time alteration	Precipitate psychoses, chromosome breaks, teratogenic potential, carcinogenic potential
Dimethyl-tryptamine (Businessman's high)	<i>Piptadenia peregrina</i> and synthetically	Injected	1 mg.	4-6 hours	Exhilaration, excitation, hallucinations	?
Mescaline (cactus, peyote)	<i>Lophophora williamsii</i>	Oral ingestion	350 micrograms, 3-15 "buttons"	12 hours	Exhilaration, anxiety, hallucinations	?
Psilocybin	<i>Stropharia cubensis</i> & <i>Psilocybe</i> spp.	Oral ingestion	25 milligrams	6-8 hours	Nausea, vomiting, hallucinations	?
Lysergic acid amides & related compounds (Morning Glory seeds)	<i>Ipomoea violacea</i> , <i>Argyrea nervosa</i> , <i>Rivea corymbosa</i>	Oral ingestion	50-500 seeds	1-4 hours	Lethargy, euphoria, hallucinations	Uterine contraction

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Uterine contraction

Lethargy,
euphoria,
hallucinations

1-4 hours

50-500 seeds

Oral ingestion

Ipomoea violacea,
Argyrea nervosa,
Rivera corymbosa

Lysergic acid
amides & related
compounds
(Morning
Glory seeds)

Many feel that useful benefits may be derived from the use of the psychotomimetics (21).

In order to understand the proposed mode of action of the mind-altering substances, it will be necessary to briefly consider the two principal theories in vogue which attempt to explain the origin of psychoses. One thesis proposes that psychological factors cause schizophrenia and other psychoses. Here, the possibility of secondary biochemical changes are not excluded. The other proposal considers that inborn or acquired biochemical abnormalities underlie psychoses. Here, the abnormal conditions cause either metabolic excesses or deficiencies. This latter proposal has support in the findings that several types of hallucinogens mimic the psychotic state to some extent.

Although little in the way of definitive results has been obtained to date, data seems to be accumulating in favor of the biochemical theory as a plausible explanation for the origin of psychosis. Whether inherited biochemical factors are implicated or crisis or stress precipitated biochemical abnormalities are the cause has yet to be clarified. Evidence exists for both.

Many investigators believe that there is a unified or basic explanation

behind the psychomolecular biology of the psychotomimetics. In fact, it was the potent effect of LSD which crystallized interest in the biogenic amines such as serotonin, norepinephrine, and dopamine, as mediators between biochemistry and human behavior.

Basically, the occurrence of these amines in the brain as possible transmitters has led to several proposals that certain abnormal metabolic derivatives can lead to the production of endogenous mind-altering substances. In Figure 4, some of the proposed substances implicated in the abnormal metabolism of epinephrine are seen. Though disputed, both adrenochrome and adrenolutin have been proposed as psychotogens (22).

In Figure 5 another proposed pathway is shown, leading from serotonin through melatonin to 6-methoxytetrahydroharman also known as adrenergolotropine. This pineal metabolite has recently been proposed as an example of the first demonstrated endogenous psychotomimetic (13). It is isomeric with 7-methoxytetrahydroharman which by coincidence is one of the euphorogens in the *Banisteriopsis* vine used by South American natives and mentioned earlier in this discussion.

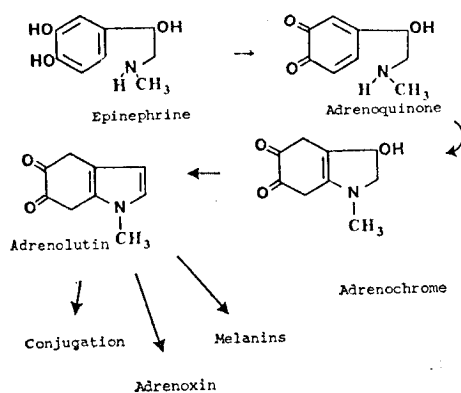


FIG. 4—PROPOSED ABNORMAL METABOLISM OF EPINEPHRINE.

The pineal gland is located above the third ventricle and is attached to the midbrain. For years, the pineal was considered to be vestigial and inactive, but recent studies have shown that it remains enzymologically active in humans right up to death (23).

It is known that the pineal gland is the only one in the body directly penetrated and thus stimulated by nerve fibers. All other glands are controlled by circulating hormones. In addition, it contains large amounts of serotonin (up to 100 ug per gram) which, as indicated in Figure 5 can lead to the production of melatonin, the major hormonal secretory product of the pineal, and thence to adrenoglomerulotropine.

Of further interest is the fact that melatonin production varies according to darkness and light via nerves that connect the pineal to the eye. Study of pineal enzymology may lead to answers to age old questions regarding biological clock mechanisms, and the various neurochemical pathways to psychotomimetics, here only hinted at.

Numerous other proposals regarding mechanism of action of the hallu-

cinogens have been made and these presented here are but one example of an early proposal and one example of a recent proposal.

Therapeutic Applications

Some of the hallucinogens, mainly LSD, mescaline and psilocybin, have found limited experimental therapeutic applications. These include:

- 1) Treatment of psychiatric conditions resistant to conventional psychotherapy.
- 2) Treatment of chronic alcoholism. (Remission rates of about 50 percent have been reported here.)
- 3) Treatment of intractable pain in patients with severe terminal or malignant diseases.
- 4) Experimental induction of psychosis in psychiatrists who wish to better understand the symptoms and feelings of patients during an attack.
- 5) Experimental induction of model psychosis in order to test new drugs for their antipsychotic activity.

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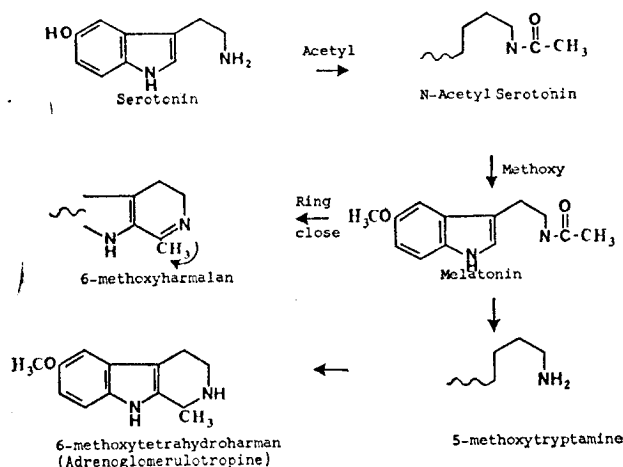


FIG. 5—PROPOSED ABNORMAL METABOLISM OF SEROTONIN.

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Although disputed, these offer some hope that certain of the psychotomimetics may have a useful place in the treatment of mental disorders (11-13).

Dangers of Misuse

No drug is without some danger and the hallucinogens are no exception. Wide extemporaneous misuse has led to the discovery that many potential dangers reside in this class of compounds. Most evidence has been with LSD and marihuana. In the former, there has been recorded, prolonged psychotic episodes, extreme anxiety, and panic reactions which have led to suicides and other bizarre reactions (19, 20). Latent effects in the form of chromosome damage, teratogenic effects, and potential induction of neoplastic diseases have also been reported.

The *in vitro* tests showed that low doses of LSD caused twice as many broken and abnormal chromosomes in leukocytes as in untreated cell cultures of these blood cells from two healthy donors. In addition, statistical evidence gathered from examination of leukocytes from individuals who were given LSD in treatment and those who were treated in a hospital for taking LSD, showed that in every case there was an increased chromosomal damage above the mean control value (24, 25).

With respect to teratogenic effects of LSD, at least one researcher (26) has described a case of a girl born with a malformed leg to a 19-year old woman who had taken LSD on the 25th day of her last menstrual period and three times between the 45th and 98th days. Her husband also partook of the drug. Since this latter time period is critical for the production of leg deformities, it was felt that it was reasonable to suspect a causal relationship between LSD intake and the fibular aplastic syndrome of the child.

While other offspring, also exposed to LSD *in utero*, were free of physical or behavioral abnormalities, they did show long lasting chromosomal damage. Based on experience with other agents producing chromosome damage, the possibility of latent deleterious effects such as leukemia developing later in life in these individuals is obvious.

In addition, the chromosome breaks induced by LSD have been found similar to those found to occur spontaneously in three autosomal recessive diseases. People with these syndromes show a high propensity to leukemia and other neoplasms.

While the current evidence is presumptive and other chemicals (e.g., caffeine) are known to cause chromosomal aberrations, the evidence does stand as clear warning of the potential dangers of these substances. Continued investigations should yield more definitive results.

Marihuana is not easy to quantitate with respect to its pharmacological properties. The variety of *Cannabis sativa* used, the environmental conditions under which it is grown, the various methods of preparation and administration, the resin quantity and quality, etc.—all ultimately affect human responses. Smoking marihuana produces effects within a few minutes which may persist for up to 12 hours.

Some of the usual acute effects seen include, a feeling of well-being, euphoria, hilarity, perverted perception and distortion of time and space, apparent intensified appreciation of art and music due to lowering of optical and acoustical sensory thresholds, irritability, confusion and impairment of judgment and memory. Danger of self-injury is obvious under these conditions.

By this mode of administration, no physical dependence or tolerance has been demonstrated. However, in

certain individuals there is a psychological dependence if it is used continuously to avoid anxiety and responsibility, or as a means of gaining social acceptance with a particular "in" group.

An expert committee of the World Health Organization has defined drug dependence of the *Cannabis* type as very clearly habit forming, though a gregarious habit and somewhat easily abandoned (28).

Those individuals who have a psychological dependence usually drift into chronic use. The chronic user of marihuana is often lethargic, slovenly in personal habits, and usually exhibits a deep sense of failure after believing that he was capable of achieving great goals. Repeated high dosages intensify the effects seen in occasional use and include more intense illusions, hallucinations and delusions that predispose to antisocial behavior, greater anxiety and aggressiveness, prolonged sleep disturbances, and recurrent psychoses. The latter effects are presumed to be due to sensory derangements (29).

Thus, it appears that the real danger of marihuana lies in its attraction to those least likely to sustain its effects; viz., those individuals who have not enjoyed a proper home life and education and those with personality defects and incipient or existing psychotic disorders. It may serve as a stepping stone to more dangerous drugs with these individuals. This drug abuse escalation is commonly seen in the urban ghettos where feelings of helplessness, oppression, powerlessness, and futile dissatisfaction are common.

Those who would argue that marihuana and LSD and the other psychotomimetic drugs are no more dangerous than alcohol or tobacco should realize that enough difficulties exist in the abuse of these to disallow addition

of further materials, particularly those which can affect the mind. There is little doubt that all the drive and goal directed energies which some of our youth possess are valuable national assets. These drugs tend to greatly affect these energies and in the process create mental and socially crippled individuals who become parasites on productive society.

Legal Aspects

The enlarging illegal traffic in the hallucinogens is posing enormous problems for the Food and Drug Administration's Bureau of Drug Abuse Control (14). The Drug Control Act of 1965 delegates to BDAC the responsibility for stemming the traffic in all the common psychotomimetics except for marihuana which the Federal Narcotics Bureau handles. Both agencies may soon merge and be transferred to the Justice Department as the Bureau of Narcotics and Dangerous Drugs.

Recently, FDA Commissioner, James L. Goddard, spoke in favor of H. R. 15355, the bill which would make a felony of the manufacture and sale of LSD and other psychotomimetics including other depressant and stimulant drugs.

The current Drug Abuse Control Amendments to the FDC Act (U. S. Code Title 21) prohibits, among other acts the following (30):

1. The sale or disposition of drugs not covered by legal prescriptions.
2. The illegal possession for resale of dangerous drugs (possession for personal use is not prohibited under Federal law).
3. The failure to register as a manufacturer or wholesaler of controlled drugs.
4. The failure to keep records of receipt and distribution of controlled drugs.

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Anyone who produces or sells dan-
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various penalties. These include:

1. First offense: a maximum pen-
alty of one year's imprisonment
and/or a \$1,000 fine.
2. Second offense: a maximum pen-
alty of three year's imprisonment
and/or a \$10,000 fine.
3. First offense for peddlers and
pushers over 18 years old who
sell or give drugs to anyone
under 21 years old: imprison-
ment for not more than 2 years
or a fine of not more than \$5,000
or both.
4. Second offense for peddlers as in
3: imprisonment for not more
than 6 years and a fine of not
more than \$15,000 or both.

Presently these agencies are encoun-
tering many difficulties in keeping up
with drug abuse problems. Much
more research is needed to supply the
kind of answers which will help all
law enforcement agencies make the
proper decisions regarding the proper
laws to fit the seriousness of the of-
fense.

Certainly the answers to many drug
abuse problems lie in continued edu-
cation of all personnel who handle
drugs and particularly all individuals
using them. Recent publications on
drug abuse problems are a good ex-
ample (31-41). Only then can proper
respect for the dangers inherent in
misuse of these potent agents be fully
realized. As has been often stated in
the past . . . the mischief lies not
in the drug itself but in the user.

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