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REPLY TO
ATTENTION OF:

December 7, 2009

Office of the Chief Counsel

Mr. John Greenewald
[redacted]

Dear Mr. Greenewald:

This is the final response to your FOIA request dated September 3, 2009 and assigned **RDECOM FOIA #FA-09-0059** where you requested a copy of the report, *Psychochemical Agents*, Accession Number AD112239, dated September 14, 1956 (enclosed).

The redacted record was subject to FOIA exemptions (b)(1), (b)(2) High, and (b)(6).

a. FOIA exemption (b)(1) protects records that are properly and currently classified in the interest of national defense or foreign policy. Two documents listed in the Bibliography remain classified.

b. FOIA exemption (b)(2) high protects substantial internal matters where disclosure would risk circumvention of a legal requirement.

b. FOIA Exemption (b)(6) along with a Department of Defense policy allows for the withholding of government employee names, email addresses, and other personal information.

Unfortunately, Appendix A, pages 14 and 15, were not readable. We scanned the enclosed pages from illegible paper copies that we received from the Defense Technical Information Center. Mr. Brian May unsuccessfully tried to enhance pages 14 and 15.

If you consider this response to be an adverse action, you may administratively appeal, in writing, to the Secretary of the Army. However, prior to appealing directly to the Secretary of the Army, I must review the appeal. Therefore, any such appeal should be addressed to this office. We will review your appeal and forward your appeal to the Army Office of General Counsel, the designated Army Freedom of Information Act appellate authority.

Additionally, if you choose to appeal, the appeal must be received by the appellant authority (Army General Counsel), no later than **60 days** following receipt of this letter. Please send correspondence to the following address:

Brian A. May
RDECOM, ATTN AMSRD-CCF
5183 Blackhawk Road, E4435
Aberdeen Proving Ground, MD 21010-5424

Fees were not assessed. Should you have any questions or concerns regarding the processing of your request, please contact Mr. Brian May at (410) 436-2289 or brian.may3@us.army.mil

Sincerely,

PATRICK R. SHELDON
Initial Denial Authority, RDECOM

Enclosures

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AD112239

Psychochemical Agents

CHEMICAL WARFARE LABS ARMY CHEMICAL CENTER MD

14 SEP 1956

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CHEMICAL WARFARE LABORATORIES

TECHNICAL REPORT

CWLR 2071

PSYCHOCHEMICAL AGENTS ~~[C]~~

by

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FC

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14 September 1956

ARMY CHEMICAL CENTER, MARYLAND

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Chemical Corps Research and Development Command
CHEMICAL WARFARE LABORATORIES
Army Chemical Center, Maryland

Chemical Warfare Laboratories Report No. 2071

Directorate of Medical Research

PSYCHOCHEMICAL AGENTS ~~(C)~~

by

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Chemical Warfare Laboratories
Report No. 2071

APPROVED:

PSYCHOCHEMICAL AGENTS ~~(U)~~

Project No.: 4-08-02-018-01
Notebook No.: None

for

ALBERT R. DREISBACH
Colonel, Medical Corps
Director of Medical Research

Date Submitted: 24 August 1956

S.D. SILVER
Deputy Commander for
Scientific Activities

[redacted]

[redacted]

(C) ABSTRACT (U)

(C) Recommendations of various Chemical Corps committees on psychochemical agents and certain criteria for the consideration of potential agents are presented.

(U) Present intramural and extramural work is reported, and emphasis is placed on the present status of the program in respect to clinical studies.

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PSYCHOCHEMICAL AGENTS ~~(C)~~

I. ~~(S)~~ INTRODUCTION (U).

~~(C)~~ During the past year a comprehensive study of psychochemical agents has been made by the Ad Hoc Study Group on Psychochemical Agents. The following quotations from the report of this group (1) serve as an excellent introduction to this report prepared for the Eleventh Tripartite Conference.

~~(S)~~ "1.1 Terms of Reference (U).

~~(C)~~ The chairman of the Research and Development Coordinating Committee on Biological and Chemical Warfare, in a memorandum dated 3 June 1955, requested the Technical Advisory Panel on Biological and Chemical Warfare to study the problem of psychochemical agents with the following terms of reference:

a. Statement of the Problem:

The Chemical Corps has been conducting a feasibility study over the past few years on agents potentially capable of producing mental changes of an incapacitating nature when administered in sublethal doses. This has involved synthesis of selected groups of compounds, animal experimentation and finally, testing of their effectiveness in humans. Concurrent work has been conducted on compounds which antidote the effects of these psychochemicals. The results indicate that psychochemicals offer promise of military value. The investigations of the Chemical Corps are at a stage which merits the advice of an outside group.

b. Recommendation:

A Study Group on Psychochemical Agents be appointed to examine the general field of chemical warfare agents that induce mental aberration and hallucination. This group will confine itself to the overt military application of these substances. The following questions should be considered.

(1) What types of psychic effects are technically feasible and for what duration can they be expected to last?

(2) What will be the probable effects on personnel?

(3) Is there sufficient promise in this field to warrant an extensive program of research and development?

(4) If the answer to (3) above is affirmative, what approaches should be considered for a reasonable research and development effort in this field?

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(U) "1.2 The Study Group (U).

The chairman of the Technical Advisory Panel appointed the following members to an ad hoc study group to conduct the requested study:

(b) (6)

(b) (6) of the OASD (R&D), acted as secretary to the group.

(U) "1.3 Meetings (U).

The Group held meetings ..... and received a series of briefings and presentations of subject matter which are attached ..... At the conclusion of the second meeting, studies were requested from various members of the Group. After the chairman consolidated the studies in draft form, the secretary visited each member of the study group and discussed the consolidated report. This formed the basis for the final-draft of the report."

~~(S)~~ The Ad Hoc Study Group proposed a detailed protocol for experimenting on volunteers and recommended that

"(1) The experiment as outlined in detail in this report, be carried out with volunteer units as soon as practicable.

"(2) The potential and promise in the use of psychochemical agents in warfare be re-evaluated upon completion of the small-unit experiments.

"(3) Increased efforts be placed on screening chemicals in the lysergic acid class to find a substitute for LSD 25.

"(4) Conditioned reflex studies, using psychochemical agents, be made on dogs and additional higher animals other than man. This should not exclude other studies of behavior.

"(5) For long-term toxication and lethal dosage studies, the dog, or similar larger animals be employed."

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(U) The author assumed responsibility for the clinical research program of Chemical Warfare Laboratories on 1 February 1956. Since then, subsequent discussion between (b) (6) and the author resulted in general agreement as to the program of research to be conducted in this field by the Chemical Corps.

~~(C)~~ It will be the purpose of this report to briefly summarize some of the more pertinent present knowledge in this field, to partially answer some of the recommendations of the advisory group, and to give an indication of the present status of the research program on psychochemicals. The authority for the proposed CmlC plant for the use of volunteers in the psychochemical program was received on 24 May 1956. This necessarily means that a considerable portion of the work on volunteer subjects must be the subject of a verbal report to the Tripartite Conference, rather than being presented in this paper.

II. ~~(S)~~ CONSIDERATION OF POTENTIAL CANDIDATE AGENTS ~~(S)~~

~~(S)~~ For practical purposes, psychochemical agents may be considered to be compounds capable of causing derangement of mental processes by one or more actions on the higher part of the central nervous system, thereby producing in humans such symptoms as anxiety, irritability, distorted perceptions of time and space, hallucinations, feelings of unreality, and disassociation from the environment. This might or might not include loss of consciousness. Such compounds may well have other physiological and pharmacological action, such as the effects upon the autonomic nervous system, but this may be of secondary importance. The criteria defined by CCTC action (2) are as follows:

"(1) Type of Action: Psychochemical agents should cause temporary mental and/or motor incapacitation (such as a state of suspended animation) of personnel.

"(2) Rapidity of Action: The agents should act promptly after administration, preferably in less than an hour. For sabotage (covert) operations, agents with delayed action (several hours) prior to onset of symptoms may be useful.

"(3) Duration of Action: It is desirable, but not essential, that the agents have no permanent effects. The minimum time for duration of action (symptoms) should be 24 hours. Agents whose action lasts for several days (even a week) may be desirable for some purposes.

"(4) Effectiveness: These agents should have a potency at least equal to the nerve gases. This means that a dosage of 0.50-0.75 mg. should incapacitate a man. This should not restrict research and experimentation on less potent compounds which may furnish data and information leading to a greater understanding of and/or better psychochemicals.

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"(5) Toxicity: These agents should have a low intrinsic toxicity; however, comparatively high toxicity should not be the basis for discarding substances having the desired incapacitating properties.

"(6) Dissemination: The agents should be capable of being disseminated in airborne form under all environmental conditions likely to be encountered.

"(7) Stability: The agents should be capable of being stored for long periods of time under all extremes of environmental conditions."

~~(C)~~ A survey of numerous compounds included within the category of potential psychochemical agents has led to a concentrated study of three prototype groups of compounds which may have value: (1) mescaline and related compounds - because of their characteristic hallucinatory effects, (2) N,N-diethyllysergamide (LSD 25) and related compounds - because of their extreme potency in producing anxiety, hallucinations, and psychoses with an unusually wide margin between doses producing mental effects and lethal doses, and (3) the active ingredients of marijuana and related tetrahydrocannabinol derivatives - because of the interesting type of long-lasting central nervous system depression seen with relatively small doses of a few of these compounds.

~~(C)~~ The attainment of various objectives in this program requires that the investigation of such psychochemical agents be paralleled by investigation of compounds potentially useful in prevention or treatment of the effects. Potential prophylactic and therapeutic compounds appear to categorize themselves into two main groups: (1) sedatives, such as the barbiturates and (2) "tranquillizers," such as chlorpromazine (2-chloro-10-(3-dimethylaminopropyl phenothiazine), reserpine, azacyclonol.

III. ~~(C)~~ INTRAMURAL BASIC AND APPLIED RESEARCH ON PSYCHOCHEMICALS ~~(C)~~.

A total of 45 compounds have, to date, been delivered to Clinical Research Division of these laboratories for study (3). These may be divided into 34 mescaline derivatives, 2 indoles of lysergic acid group, 1 aniline derivative, and 8 tetrahydrocannabinols. The mescaline group is most usefully subdivided according to the number and location of methoxy groups on the benzene ring. One group of eight of these compounds has a methylenedioxy linkage rather than two methoxy groups.

IV. ~~(C)~~ TOXICITY STUDIES (U).

Of the total group of 45 compounds, 22 have been investigated for toxicity to the extent of determining LD50's in at least five species of animals. An additional 14 compounds have been investigated for toxicity to the extent of determination of LD50 by intraperitoneal injection in mice. Part of

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this work was done under contracts DA-18-108-CML-3968 and CML-5663, with the University of Michigan, the principal investigator being (b) (6) Part of the work was done in Field Toxicology Branch and a further portion by personnel of the Neurology Branch of these laboratories. These data, together with the identifying numbers of the compounds, and their structural formulae have been compiled in table 1. The reference note given at the extreme right of the table indicates the laboratory in which the work was done and the report where details may be found.

V. ~~(C)~~ COMMENTS ON TOXICITY INFORMATION ~~(C)~~

The information in table 1 represents 120 LD50 determinations on 36 different compounds in one or more of five species of animals and represents the total utilization of more than 5,000 animals. When sufficient information has been obtained to permit the calculation of the ratio of the effective dose as compared to the lethal dose, the value of this ratio will then permit selection of further compounds for study. It must be understood that no compound is accepted or rejected for further study on the basis of toxicity determination alone.

Examination of the table indicates that there is no single species which is consistently more sensitive or less sensitive to these compounds. For economic reasons the number of LD50 determinations in monkeys and in dogs is somewhat less in this series. Examples can be cited where all species show approximately the same sensitivity to a compound, and other examples could be cited where the lethal dose in one species is as much as ten times the comparable dose for another species even though the route of administration is the same.

Except for the tetrahydrocannabinol derivatives, almost all of these compounds produce convulsions before death. In many cases, hypersensitivity to stimuli, hyperactivity, tremors, or ataxia are reported. The three tetrahydrocannabinol derivatives which have thus far been studied (b) (2) High (b) (2) High all produce a depressant type of response in the animals thus far studied. Compound (b) (2) High is conspicuous for its long duration of action. Behavior suggestive of hallucinations has been reported in dogs given (b) (2) High (b) (2) High and possibly (b) (2) High In cats the phenomenon has been observed following (b) (2) High . In monkeys this is reported after the administration of (b) (2) High and difficulty in vision is reported in monkeys who have received (b) (2) High

Pharmacological and physiological action of these compounds is being studied under extramural contract and in three other branches of our Medical Research Directorate. The Comparative Physiology Branch is developing techniques for screening psychochemical compounds on a large variety of species of animals. The Psychology and Human Engineering Branch is conducting.

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behavioral studies on animal's ability to perform certain tasks under the influence of certain of these agents. Neurology Branch is conducting a prolonged study of acute and chronic dosages in rhesus and spider monkeys.

In order to study the localization of effects of these agents on the central nervous system, the method described in previous conferences using the so-called transcallosal preparation, which is a method of studying the effect of transmission of nerve impulses in the animal brain, has been used (4). In order to correlate and compare the accuracy of this type of preparation, a more commonly accepted spinal segmental reflex preparation in the cat has been used for study. Evidence at this time using this preparation indicates that (a) mescaline, given in concentrations of 2.5 to 5 mg./kg. has a primary action of inhibition, (b) facilitation is present in most of the preparations studied, and (c) the drug seems to be as effective in the same range of dosage on the cord preparation as in the cortical preparation.

VII. ~~(C)~~ CLINICAL STUDIES (U).

~~(C)~~ Neurophysiological, biochemical, histological, and clinical pathological studies of these compounds on both man and animals are very important in the guidance of this group. The amount of literature is tremendous, particularly on the subject of LSD, some of its analogs, and various so-called "tranquilizing" compounds.

~~(C)~~ From the recent stimulus in the field on this subject, it would seem that many research laboratories now have departed from the overworked epinephrine-adrenaline field to this field of 3-(2-aminoethyl)-5-indolol (serotonin) and its related structures.

(U) This is not a statement of disparagement, but rather to point out the vast interest in fundamental research on these compounds, which undoubtedly will greatly improve our understanding of some of the fundamental processes of the central nervous system. In light of this, it would seem unfitting to launch upon a large-scale basic mechanism study of such compounds, but rather to concentrate attention on two compounds of interest in the light of current military needs.

~~(C)~~ If one is also aware of the vast clinical psychiatric experience in the field of mescaline and LSD type of compounds, he becomes smothered by the preponderance of conflicting reports. However, through this maze of clinical reports, methods, techniques, and clinical laboratory findings, certain information becomes evident.

(C) In choosing two different representative compounds, (b) (2) High and (b) (2) High, for close study, some better compounds may well have been overlooked. If these compounds do not measure up to expected results, it is in no way an indication that the whole program should be abandoned.

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(U) It has been repeated often in the literature that if most subjects are given enough of one of these compounds certain things happen, some of which are observable and others which can be only detected by objective testing. Responses are dependent on the personality complex, the present physical and mental status, the dosage administered, the environmental conditions, and very probably, the subjects' knowledge that they received or may possibly have received a drug.

~~(C)~~ [redacted] in an oral effective dose range of 0.5 to 5 gamma/kg. (35-350 gamma/70-kg. man) produces physiological and psychic changes which may either be measured and/or observed. The onset of action is usually within 1/2 hr., and the duration of action may persist for as long as 8 hr. or more but usually is of shorter duration.

~~(C)~~ [redacted] (tetrahydrocannabinol type) in oral doses from 10 to 70 gamma/kg. produce marked hypotension and often psychic manifestations which may persist for as long as 24 to 48 hr.

~~(U)~~ The human toxicity data available to date indicate a wide safety margin between effective and lethal doses.

VII. ~~(C)~~ MM 1605 VOLUNTEER PROGRAM (U).

(U) The clinical program of these laboratories is designed to obtain as many subjective and objective measurements as is practicable. Therefore, it is divided into several phases.

(U) Phase I, Evaluation of the Individual Subject (U).

A. Physical Examination.

1. General
2. Neurological
3. Chest X-ray
4. EKG
5. EEG
6. Hemogram

B. Psychiatric Evaluation.

The clinical psychiatrists assess the following points:

1. Early and present family structures and position of the subject within the structure; feelings about relatives, parents, and

siblings, identification with adult figures and attitude toward family members; feelings about persons in authority.

2. Educational, social, and economic background and experiences.

3. Significant life experiences - military, occupational, religious.

4. Modes of adaptation; strivings and goal seeking; inhibitions and methods of dealing with them; reactions to failure and inadequacy (denial, repression, depression, hostility, etc.); reactions to success and achievement; use of alcohol, tobacco, and drugs.

5. Attitude towards the experimental procedures; motivations for taking part in the experiment.

6. Primary motivations, inhibitions, suggestibility and reaction to the experimental physician and the environmental surroundings.

7. Existence of psychopathology - motivation in taking part in experiment and attitude toward it.

C. Psychological Evaluation.

1. Tests designed to determine the subject's personality structure are given by the clinical psychologists. These include such tests as the Rohrschach, MMPI, Goldstein-Scharer, Halstead Category Test, Thematic Aperception Test, and others.

2. Intelligence tests, such as the Wechsler-Bellevue test, are used.

3. Tests to detect alteration in sensory perception, determination of reaction time to visual and/or pain stimuli, the critical flicker fusion test, and the estimations of visual and auditory thresholds are of value for providing criteria of the effects of the drug on the sensory system.

(U) Methods of Dosage Administration and Observation Periods (U).

Oral routes are used, except under certain specific circumstances. The double blind method of administration is utilized throughout. The dosage ranges are within the previously stated levels. All personnel are attended on a 24-hr. basis by physicians and medically trained personnel throughout the testing periods.

(U) Phase II, Group Studies (U).

This phase will involve interaction within small groups of four men with concomitant studies of the foregoing nature, in addition to which group interaction and response is noted.

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~~(C)~~ Phase III (U).

This is divided into two parts. In the first part, organized groups with recognized leaders will be subjected to various problems of intelligence, memory, interrogation, and highly skilled manipulative procedures. They will be placed in varying positions of responsibility, under varying conditions of having the leader receive the drug alone, their receiving it and not the leader, and many variations of such procedures.

The second part will use larger groups, with recognized functions of command. This may include such things as the action of a firing battery or a mortar group. It may be the function of part of a NIKE installation; and it will include, if feasible, operations including those of Navy, Marine, and Air Force personnel. Future plans, depending on concurrence by Departments of the Navy and Air Force and their Surgeons General, call for tactical Air Force crews who have been well integrated as functioning units to undergo experimental procedures. It is also hoped that small cadres of Fleet Marine Force combat-trained troops might be used for selected field tests.

VIII. ~~(C)~~ ADDITIONAL CLINICAL STUDIES (U),

(U) In correlation with the above, critical studies are made of biochemical and histological alterations of the blood and its components. Studies are made of electrolyte balance and of urinary excretory function, including both normal and stress metabolities.

~~(C)~~ Additional information of value is gained from sources of schizophrenic patients with permanent subcortical electrodes. In this manner repetitive examinations of brain wave patterns using a number of compounds at varying dose ranges in the same individual have been made possible.

(U) In the field of prophylaxis and therapy, several sources of information of clinical trial have been made available. This information is utilized wherever possible and when necessary extramural contractors have undertaken more intensive clinical studies on such prophylactic and therapeutic agents.

~~(C)~~ Six supporting institutions are doing specialized work under contract, at the present time, in this field to supplement efforts on this program both from the agent aspect and also from the prophylactic and therapeutic standpoints.

IX. ~~(C)~~ DISCUSSION (U).

There are many other compounds that have been studied quite intensively and show promise in the psychochemical program, but which have been deleted from future concentrated study because they do not meet the criteria

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of dosage, solubility, or stability in solvents or as aerosols. Mescaline is an example of a drug which requires large doses (500 mg.) and is not stable. α-Chloralose, though requiring similar doses for effects in humans, might well be considered as a possible screening or interrogative type of comp and (5). Alkaloids are expensive and usually very difficult to synthesize. Certain analogs of LSD25 are promising but are in the preliminary stage of animal experimentation. Structural relationships among some of the psychically active compounds that are of interest to these laboratories are indicated in appendix A.

A word of caution to those who would like to see immediate large-scale experiments conducted in this program. (b) (2) High

(b) (2) High

(b) (2) High This is one of the principal deterrents to attempting tasks as outlined by the Ad Hoc Study Group on Psychochemicals. Such tasks might well get out of hand despite elaborate precautions.

It has been shown that in animal experimentation there is no single species which is consistently more or less sensitive to these compounds. However, examples can be cited where all species show approximately the same sensitivity to a compound, and other examples are noted where the lethal dose in one species is as much as ten times the comparable dose for another species even though the route of administration is the same. Certainly within the same species there may well be considerable variability. There are various reasons for believing that man has varying tolerances to these compounds. The human organism is the most complex structure known. Man is also the most reactive to his environment. Most of his reactions occur automatically through his sensory perceptive systems and his autonomic nervous system, and reflexly through part of his central nervous system without his conscious thought. The greatest advantage he possesses over other animal life is the enormous complexity of functions of the cerebral cortex and related structures. Certainly it must be admitted that there is great variability among men in the functional response of the "psyche." If these compounds alter certain sensory and somatic systems such as auditory, visual, and position sense to a variable degree in different individuals, then one might also expect that the psychic manifestations exhibited under the influence of the drug might also vary depending on such things as personality complex, present physical and mental status, and the environmental conditions. It is reported that both man and animals do acquire tolerance to daily administration of some of these compounds, but this tolerance disappears within 3 days after discontinuation of the drugs (7). These are a few of the problems presented in this program.

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X. ~~(C)~~ RECOMMENDATIONS (U).

It is recommended that the psychochemical program be continued by the United States at the maximum practicable rate. (b) (2) High

(b) (2) High

XI. ~~(C)~~ BIBLIOGRAPHY (U).

(b) (1) (A)

3. ~~(C)~~ E. Ross Hart, CWLR 2021, Psychochemical Program, Status Report as of 31 December 1955, 3 May 1956.

4. (U) Conference on the Pharmacology of Psychotomimetic and Psychotherapeutic Drugs; New York Academy of Science, April 12-14, 1956.

5. (U) Tulane University, Contract Report DA 18-108-CML-5595, April 1956.

6. (U) C. Elkes, J. Elkes, and W. Mayer-Gross, Hallucinogenic Drugs, Lancet 268, 719 (1955).

7. (U) H. Isbell, H.F. Fraser, A. Wikler, and R.E. Belleville, Tolerance to Diethylamide of Lysergic Acid (LSD-25) Fed. Proc. 14, 354 (1955).

APPENDIX A

TABLES

Table 1-A

Toxicity of Psychochemicals
LD50 mg./kg. (19/20 Confidence Limits)

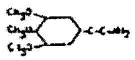
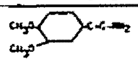
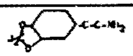
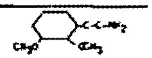
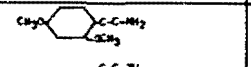
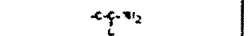
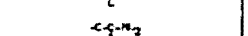
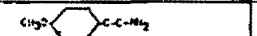
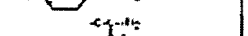
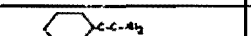
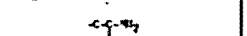
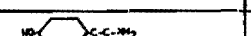
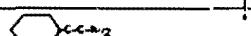
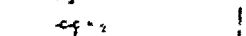
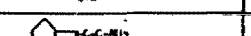
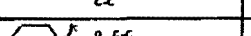
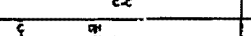
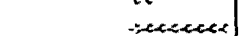
EA No.	Formula	Mouse I.P.	Rat	Guinea Pig I.P.	Rabbit I.V.	Cat I.V.	Dog I.V.	Monkey I.V.	Reference
1336			I.V. 130 (115-140)		200 (157-254)	155 (125-189)			Hearst
		220.0 (200-242)	I.P. 132 (104.3-164)	370 (301.4-464)			54.6 (46-64)	140.0 (115-169)	Mich 4
1319	-C-C(C)-NH2	240 (222.2-259)	I.P. 149 (141.9-156.4)	172 (159.2-185.7)			22.0 (15.0-33.0)	31.0 (25.0-38.4)	Mich 4
1506	-C-C(C)(C)-NH		I.V. 23_ (113-16_)		79 (66.1-92.5)	79 (68.0-91.6)	115 (86-154)	63.0 (56.5-73.4)	Tox 3
1505	-C-C(C-C)-NH2		I.V. 94.2 (82.6-107)		63.0 (55.0-71.8)	71 (58.2-86.4)	48 (37.2-61.9)	71 (58.5-86.0)	Tox 2
1554	-C-C(C)(C)-NH2		I.V. 64 (53.7-76.1)		63 (53.4-74.3)	63 (54.3-71.8)	88.0 (70.9-109.1)	63 (52.0-76.2)	Tox 8
1536	-C-C(C)(C)-NH-C		I.P. 106 (101-111)		56 (51-62)	77 (66-89)	106 (95-119)	52 (43-62)	Tox 7
1296		263 (241-286)	I.P. 160 (120-212)	390 (364-417)			122 (109-136)	240 (175-330)	Mich 5
1316	-C-C(C)-NH2		I.V. 47.3 (41.2-54.5)		45.2 (38.2-54.5)	107.2 (94.4-126.5)	46.0 (32.0-72.8)	40.0 (31.4-53)	Tox 5
		168.0 (157-180)	I.P. 48.0 (41-57)	198 (156-234)			59.0 (52-67)	53.0 (46-61)	Mich 6
1322	-C-C(C-C)-NH2		I.V. 71.0 (63.2-79.6)		54.3 (46.3-66.0)	88.0 (75.9-102)	74.5 (64.5-91.0)	50.2 (44.5-58.0)	Tox 4
		192 (187-197)							Mich 2
1297		176.3 (163-190)	I.P. 55.0 (42-72)	245 (206-292)			28.3 (25-32)	45.0 (40-51)	MFG 6
1298	-C-C(C)-NH2	57.7 (43.3-77.0)	I.P. 33.1 (22.0-48)	33.7 (26.9-42.3)			6.8 (4.6-9.8)	9.6 (6.0-13.5)	Mich 4
1300	-C-C(C)-NH2	7_ (60-89)	I.P. 95.0 (42-100)	100.0 (65-154)			16.0 (10-24)	26.9 (13-33)	Mich 5
1503	-C-C(C)(C)-NH2		I.V. 20.9 (16.6-26.2)		17.0 (13.6-21.3)	2_.6 (16.6-27.2)	36.6 (31.3-42.5)	20.0 (17.3-23.3)	Tox 1
1475	-C-C(C)(C)-NH	97.0 (88.5-106)	I.P. 46.0 (33.3-66.2)	96.0 (85.0-111.2)			16.0 (8.4-23.1)	22.0 (17.6-27.3)	Mich 3
1537	C-C(C)-C(C)-N (Low melt.)		I.V. 33.2 (28.7-38.3)		29.5 (22.6-33.8)	32.6 (27.3-38.9)	56.2 (48.6-66.1)	23.5 (_.1-26.7)	Tox 6
1538	C-C(C)-C(C)-N (High melt.)		I.V. 32.2 (26.1-39.6)		25.4 (20.0-31.1)	_1.5 (41.6-42.2)		26.1 (20.7-33.0)	Tox
1315			I.V. 3_ (28.6-39.0)		50.0 (43.3-57.5)	55 (48-6_)	"Incomplete"	"Incomplete"	Hopfel
1305	-C-C(C)-NH2	105 (100-110)							Mich 2
1320	-C-C(C-C)-NH2	73 (69-77)							Mich 2

Table 1-B

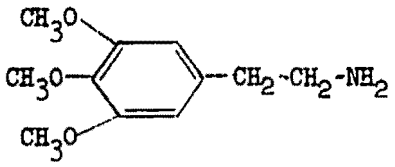
EA No.	Formula	m.p. or b.p.	Rat	Guinea Pig i.p.	Rabbit i.v.	Cat i.v.	Dog i.v.	Monkey i.v.	Reference
1321		165 (158-171)							Mech 2
1322		109 (90-120)							Mech 2
1324		94 (86-102)							Mech 2
1291		63 (60-66)							Mech 2
1314		81 (71-91)							Mech 2
1302		90 (76-104)							Mech 2
1305		45 (41-49)							Mech 2
1290		>100							Mech 2
1312		220 (216-224)							Mech 2
1313		110 (97-123)							Mech 2
1325		85 (80-90)							Mech 2
1539			i.v. 0.7 (0.6-0.8)		17.0 (8.5-16.0)	5.6 (4.4-7.2)	6.4 (7.7-9.2)	5-10*	Neurol
1540			i.v. 32 (25-42)		25 (19.5-32.2)	25 (20.6-31.3)	26.5 (21.3-28.2)	*incomplete	Neurol
1531			i.v. 59 (50.6-69)		160 (150-170)	69 (70-100)	Supply exhausted		Neurol
1477		>2000	i.v. >2500				120 (total in one dog	112 (only 2 monkeys used)	Mech 5
1476		390 (360-360)					50-100*		Mech 5
1466		2100 (1615-2720)					>200	>5	Mech 5

UNCLASSIFED

APPENDIX B

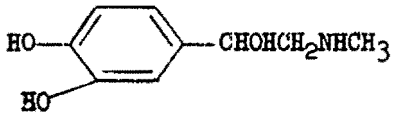
STRUCTURAL RELATIONSHIPS AMONG SOME PSYCHICALLY ACTIVE COMPOUNDS ~~(C)~~

1. (U) Phenethylamine Derivatives (U).



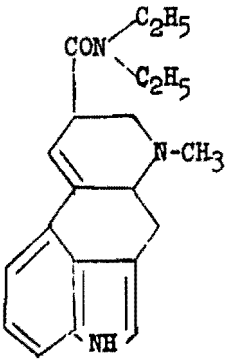
Mescaline

In studying modifications of this structure, the number and position of the methoxyl groups were varied, and the side chain was altered in some cases by substitutions of small groups.

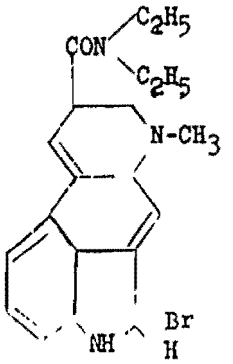


Adrenaline

2. ~~(C)~~ Indole Derivatives (U).



N,N-Diethyllysergamide (LSD)



2-Bromo-N,N-diethyllysergamide (BOL)

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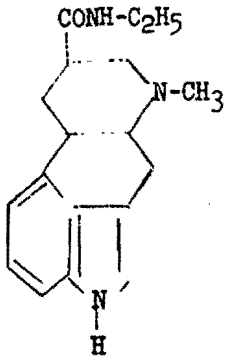
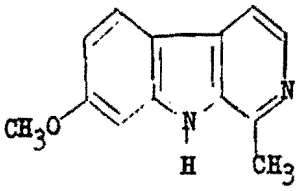


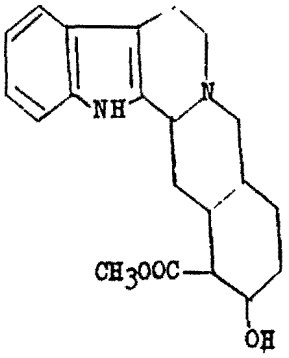
N-Ethyllysergamide (LSM)

Less complex structures related to LSD are under investigation. Among these are simple indole ethylamine derivatives and mono-, di-, and tricyclic compounds related to fragments of the LSD structure.

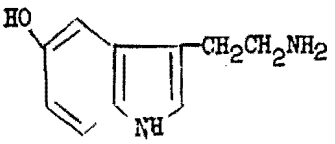


Harmine

This substance is said to be a potent intoxicant and hallucinating agent. Its structural relation to LSD (above) and yohimbine (below) is apparent.



Yohimbine



3-(2-Aminoethyl)-5-indolol (serotonin)

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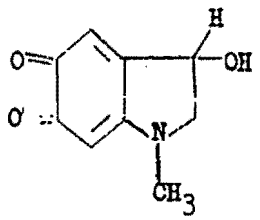
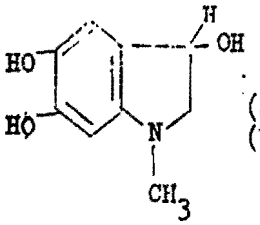


(a)

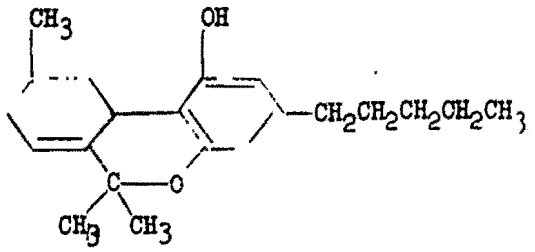


(b)

(a) Adrenochrome
(b) 1-methyl-3,5,6-indoletriol (adrenolutin)

Adrenochrome is an oxidation product of adrenaline and might be considered as showing a biochemical link between the indole and the phenethylamine type of mentally active substances.

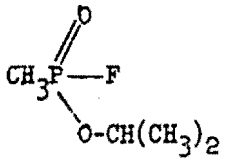
3. ~~(C)~~ Benzopyran Derivatives (U).



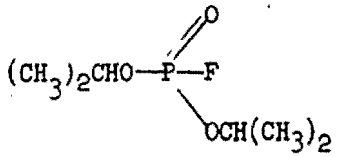
Tetrahydrocannabinol

This is the active constituent of marijuana. Several modifications of this structure were prepared, including the potentially valuable one (EA 1476) in which the C_5 side chain is replaced by 1,2-dimethylheptyl ($-CH(CH_3)-CH(CH_3)-CH_2CH_2CH_2CH_2CH_3$) group.

4. (U) G-Type Agents (U).



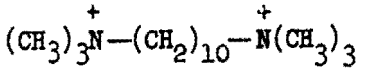
Isopropyl methylphosphonofluoridate (GB)



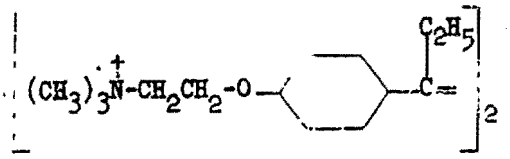
Diisopropyl phosphorofluoridate (DFP)

5. (U) Curare and Related Synthetic Paralyzing Agents (U).

d-Tubocurarine is a complicated quaternary bisbenzylisoquinoline alkaloid. Its paralyzing properties are duplicated to some extent in some simplified bis-quaternary amines. The following structures are typical:

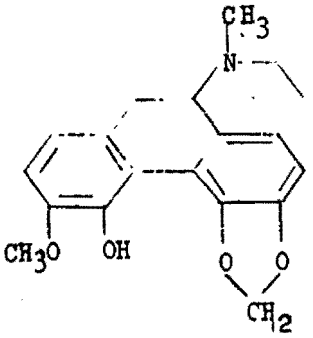


N,N,N',N'-Tetramethyl-1,10-decanediamine, alkyl halide salts and others



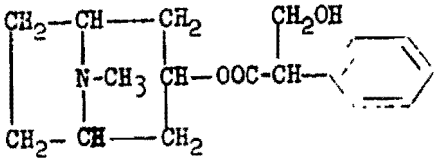
Alkyl halide salts of the 4,4'-bis(2-dimethylaminoethyl) diether of α,α'-diethyl-4,4'-stilbenediol

6. (U) Substances Related to Bulbocapnine (U).



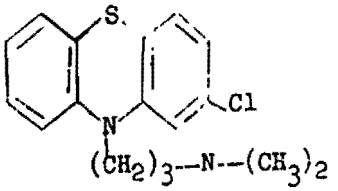
Bulbocapnine

7. (U) Substances Related to Belladonna Alkaloids (U).

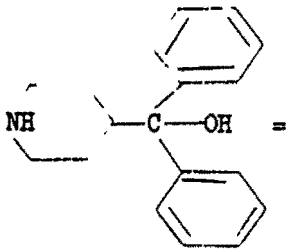


Atropine

8. (U) Tranquillizing Agents (U).

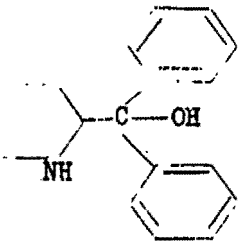


2-Chloro-10-(3-Dimethylaminopropyl)-phenothiazine (chlorpromazine, thorazine, lactargil)



= δ isomer of meratran

α,α-Diphenyl-4-piperidinemethanol
(frenquel)



α,α-Diphenyl-2-piperidinemethanol

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