THE BLACK VAULT

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[illegible]

Background and Chemistry

Through Dr. Schultes of Harvard University, the mushroom "Teonanactl" of the Aztecs was brought to our attention as having CNS stimulant properties. Although the literature claims this to be Panaeolus campanulatus, it has been learned that a larger one, Psilocybe is the mushroom responsible for the stimulant and hallucinogenic action. Samples of Panaeolus and another unidentified CNS stimulating mushroom were sent to us by Mr. Palacios-Rincon via Mr. John Klopfer, Mexico. The Panaeolus showed no appreciable activity, but the unidentified material was classified as Psilocybe mexicana which is the one the Wassons claim is used for stimulation by the Indians. Discussions have been held with Mr. Gordon Wasson who has published the results of his expeditions in search of the hallucinogenic mushrooms. At present, Dr. Moore of the University of Delaware, a contact of ours as well as one of the group with Mr. Wasson, is working on extracts of Psilocybe for us.

Extraction of the dried ground mushrooms with [illegible] ethanol at room temperature followed by concentration in vacuo at temperatures below [illegible]°, extraction with hexane, and finally lyophilization yields approximately [illegible] of water-soluble resinous solid ([illegible]), giving trace alkaloid tests with Mayer's reagent.

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[illegible] Psilocybe caerulescens.

[illegible] 677, [illegible] psychotomimetic or biological effect in animals. The following is a report of our findings:

1. [illegible] produced activity in [illegible] mice [illegible] increased activity after doses of [illegible] mg/Kg. In [illegible] these levels above 200 mg/Kg, the animals [illegible] and sound. No lethal effects [illegible] up to 700 mg/Kg.

↓ ACTIVITY
↑ INCOORD

2. Blood pressure:

In the normotensive rat, [illegible] produced [illegible] pressor responses following [illegible] doses of 1.0 to 20 mg/Kg. A mild dose response effect [illegible] was observed in one experiment at high dose levels, it appears that [illegible] No. 677[illegible] failed to have a [illegible] effect on the [illegible] pressure. It may be interesting to mention here that Psilocybe differs from Mescaline or LSD in that the latter two substances are [illegible] agents in the anesthetized [illegible] clinically [illegible] Hoffman.

3. Antagonism: [illegible] No. 677 was devoid of antipsychotic activity in the [illegible] dose [illegible] mg/Kg, I.V.

4. Antiepileptic: [illegible] No. 677 [illegible] prevent or alter PTZ seizures in mice [illegible] 100 mg/Kg, I.P.

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[illegible] of December 9, 1957 on
[illegible]

[illegible]

[illegible]

[illegible] Effect on [illegible] in Rats (P.O. & I.P.) — [illegible] escape response

[illegible]. Dose [illegible] in [illegible] [illegible]

In dogs doses [illegible] to produce significant behavioral changes. At [illegible] mg/Kg, apprehension, panting, mydriasis and [illegible]. At the 25 mg/Kg level, restlessness, vocalizing, mydriasis, [illegible] and apprehension were evident. Our impressions in this study [illegible] subjective. No obvious changes in behavior were apparent although at times the observers thought that slight behavioral changes were noted; however, these equivocal effects indicate that our recorded observations may be questioned. In the monkeys, intravenous doses of 25 or 50 mg/Kg failed to produce behavioral changes or significant side effects. It should be mentioned here that this sample of SKF No. 6778 had been in the laboratory for four months and may have lost potency.

Overall Summary:

It is apparent from the data presented that we were not able to demonstrate any unusual pharmacologic activity after administration to rats and mice. SKF No. 6778 failed to antagonize [illegible] (in contrast to LSD) and did not produce any characteristic effects such as those seen after administration [illegible] (scratch phenomenon).

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[illegible] Table I

1 - Dogs

Dose (mg/Kg)	Observations
10	[illegible], salivation, panting, apprehension
25	mydriasis, [illegible], vocalizing, slight salivation, apprehension, no effect on appetite.

2 - Monkeys

Dose (mg/Kg)	Observations
25	no side effects
50	Deep increased respiration on injection, mouth movement

B. Psilocybe [illegible] - Sample No. [illegible] submitted to E. Macko on 2/11/58 by Dr. I. [illegible]chter

1. Dose Range in Dogs

Intravenous doses of 25, 50 or 75 mg/Kg were administered to each of three dogs respectively. After injection all of the dogs exhibited side reactions; however, whether these reactions are indicative of behavior changes could not be determined with certainty. At the 25 mg/Kg level, [illegible] alternate [illegible] and apprehension, jaw movement and [illegible] were observed. In addition, this animal sat quietly, [illegible], raised his head toward [illegible] looking for something. [illegible] following injection. A dose of [illegible] lasted 30 minutes following

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[illegible] for a five hour observation period. A dose of 75 mg/Kg produced salivation, diarrhea, ataxia, stiff lameness, dilated pupils, jaw movement, apprehension, body shakes and an initial transient stimulation. Further, this dog appeared to be looking for something and stood facing the back of the cage for three to four hours.

In these animals, SKF No. 5775 produced visible biological side effects following doses of 25 to 75 mg/Kg, intravenously.

One can only speculate about the connection of these effects and the hallucinogenic effects reported in man.

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2. Daily administration of SKF No. 6778 (Sample No. 2) in Dogs and Monkeys

In order to attempt to produce more definitive hallucinogenic or biological activity, daily administration of SKF No. 6778 was initiated in dogs and monkeys for five days with the following dose schedule.

Species	Days. Dose (mg/Kg) 1	2	3	4	5
Dog 2,3,5	25 (i.v.)	→	50 (i.v.)	200 (i.v.)	800 (oral)
Dog 4, 6	100 (oral)	→	200 (oral)	800 (oral)	"
Monkey 28, 43	25 (i.v.)	→	50 (i.v.)	200 (i.v.)	"

Our data is summarized in Table III.

Results:

No significant changes in the behavior of the monkeys was observed from daily doses of 25 to 200 mg/Kg of SKF No. 6778, intravenously, for four days followed by one dose of 800 mg/Kg, orally, on the fifth day.

In the dogs, questionable behavioral changes were observed in some of the animals (Dogs No. 5, 6) in doses below 200 mg/Kg, intravenously. However, doses of 200 mg/Kg, intravenously or 800 mg/Kg, orally, produced considerable side effects which were characterized by ataxia, crying, apprehension, tremors, mydriasis, etc. As shown in Chart III, it appeared to the observer that the side effects after 800 mg/Kg, orally, were more intense than those following 200 mg/Kg, intravenously. Therefore, on the fifth and last day all of the animals received 800 mg/Kg of SKF No. 6778, orally. In the dogs, certain as well as significant behavioral changes and side effects were observed. The gross observation autopsy of 2 of the dogs 4 days after the last dose revealed no discrete tissue damage.

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Table III

Daily Administration of Psilocybe caerulescens in Dogs and Rabbits

1 [illegible]: 25 mg/Kg (i.v.)	2 25 mg/Kg (i.v.)	3 50 mg/Kg (i.v.)	4 200 mg/Kg (i.v.)	5 800 mg/Kg (p.o.)	Observations [illegible]
Side effects: intermittent and tr[illegible] crying	slight salivation	No side effects	sl. salivation after injection, slight dyspnea, mydriasis, ataxia for 3 hrs., normal in 6 hrs.	vomited part of dose in 20 min. quiet recovery	[illegible]
No side effects	No side effects	no side effects	ataxia, apprehension, cowering in corner, crying excited, dyspnea apprehension > 6 hours	vomited partial consult 15 min. after dose, nausea, crying, vocalizing for 45 min., depressed for 2 hours	Extremely [illegible] end of [illegible] 18 days
barking, crying, very excited, mydriasis, panting, jumps to one side of cage for 12 min. crying for 40 min.	barking, vocalizing, excited very excited when approached can be calmed down	barking, excited	barking, excited	ataxia, leans against cage door, presses nose thru slits, almost a TZ effect in leaning against cage	Very friendly, [illegible] jumps around, only slightly apprehensive
Dose: 100 mg/Kg (p.o.) No effects	100 mg/Kg (p.o.) No effects	200 mg/Kg (p.o.) No effects	800 mg/Kg (p.o.) crying, vocalizing for 1 hr., mydriasis, watery eyes, depressed [illegible]	800 mg/Kg (p.o.) apprehensive, crying, for 1 hr., ataxia, depressed > 1 hrs.	friendly, hyperactive

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	1 Dose: 100 mg/Kg (p.o.)	2 100 mg/Kg p.o.	3 200 mg/Kg (p.o.)	4 800 mg/Kg (p.o.)	5 800 mg/Kg (p.o.)	Observations before [illegible]
[illegible] 8	[illegible] crying, panting	no effects	crying, whining, can be interrupted	panting, muscle ripple or spasm on thigh tremors crying 15 min. howling 1 hr. depressed 3 hrs. normal 6 hrs.	vomited part of capsule in 20 min. depressed 1 hr., normal in 3 hrs.	Very friendly [illegible] tried to [illegible] aggressive, [illegible] active
[illegible] 23	Dose: 25 mg/Kg (i.v.) deep respiration on injection transient drooping of eyelids, mouth movements 2 1/2 hrs.	25 mg/Kg (i.v.) deep respiration on injection	50 mg/Kg deep resp. on injection mouth movement 5-10 min.	200 mg/Kg (i.v.) deep resp. on injection mouth movements apprehensive, tremors, head movements	800 mg/kg (p.o.) mouth movement (?)	Very aggressive
[illegible] 13	deep respiration on injection transient droop of eyelids	deep resp. on injection	deep resp. on injection	deep respiration on injection	mouth movement (?)	Very aggressive

Conclusion:

Psilocyba caerulescens produced side effects and some behavioral changes in dogs following massive doses of 25 to 200 mg/Kg intravenously or 100 to 800 mg/Kg, orally. Although our observations are purely subjective and can lead only to speculation concerning the hallucinatory effect of this substance in man, we have established that Psilocybe caerulescens should be relatively non-toxic.

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