

## References and Notes

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3. Abbreviations: Ap, adenosine 3'-phosphate; Cp, cytidine 3'-phosphate; DiHUp, 5,6 dihydrouridine 3'-phosphate; DiMeGp, N<sup>2</sup>-dimethylguanosine 3'-phosphate; Ip, inosine 3'-phosphate; MeGp, 1-methylguanosine 3'-phosphate; Melp, 1-methylinosine 3'-phosphate;  $\psi$ p, pseudouridine 3'-phosphate;  $\psi$ l, pseudouridine 2', 3' cyclic phosphate; Tp, ribothymidine 3'-phosphate; tRNA, transfer RNA; Up, uridine 3'-phosphate.
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## 2,5-Dimethoxy-4-methyl-amphetamine (STP):

### A New Hallucinogenic Drug

**Abstract.** *We have assessed the effects in normal control volunteers of 2,5-dimethoxy-4-methyl-amphetamine, the chemical present in the hallucinogenic drug STP, in two independent trials. In low doses, this compound produces a mild euphoria. Doses greater than 3 milligrams may cause pronounced hallucinogenic effects lasting about 8 hours and similar to those produced by hallucinogenic doses of lysergic acid diethylamide, mescaline, and psilocybin. 2,5-Dimethoxy-4-methyl-amphetamine, which is chemically related to mescaline and amphetamine, is about 100 times more potent as a hallucinogen than mescaline and only one-thirtieth as potent as lysergic acid diethylamide. Its psychological effects are not accentuated by chlorpromazine.*

A new hallucinogenic drug, STP, has been used extensively by "hippie" populations in recent months. There have been reports that this drug produces hallucinogenic reactions lasting up to 72 hours and that these reactions are intensified by chlorpromazine, the tranquilizer commonly used as an antidote to other hallucinogens. Chemists at the U.S. Food and Drug Administration have identified black-market preparations of STP as identical with DOM (2,5-dimethoxy-4-methyl-amphetamine) and have estimated that black-market preparations of this drug contain about 10 mg of DOM in each pill (1). To clarify the effects of DOM in man, we have, at the request of the Food and Drug Administration, examined the physical and mental actions of DOM in normal control volunteers. Two independent studies have been performed, one at the Johns Hopkins Hospital in Baltimore and one at the Veterans Administration Hospital in Palo Alto, California.

Five normal control male volunteers aged 21 to 35 were obtained through

the office of financial aid at the Johns Hopkins University. They were interviewed by an experienced clinical psychiatrist (L.F.) and were administered a Minnesota Multiphasic Personality inventory and a Thematic Apperception Scale. Applicants with a history of frequent use of marijuana or other mental stimulants were rejected. Before receiving the drug, each subject was given a physical examination, chest x-ray, electrocardiogram, electroencephalogram, tests of blood chemistry, and hematological tests. Subjects were told that they would receive a drug called DOM, which was presumably identical to the hallucinogen STP, but that their dose would be considerably smaller than that thought to occur in STP tablets.

At 9 a.m., after fasting since the preceding midnight, subjects received DOM at dosages of 2.0, 2.4, 2.4, 2.8, and 3.2 mg as the hydrochloride dissolved in distilled water. Before receiving the drug and 2, 4, and 6 hours thereafter, tests of free recall, associative organization, subjective mood

scales, and an LSD symptom specific scale were administered. Results of these tests will be reported separately (2). Urine collections before administration of the drug and 3, 6, 9, and 24 hours thereafter were assayed for unchanged DOM by a specific and sensitive spectrophotofluorometric method (3). At hourly intervals, pulse, blood pressure, oral temperature, and pupillary diameter were measured. Interviews with subjects were tape-recorded at various intervals.

Pupillary dilatation of about 15 percent occurred between 1 and 6 hours after administration of the drug. Pulse rate increased (mean increase of 15 beats per minute) as did systolic blood pressure (mean increase of 15 mm-Hg) between 1 and 6 hours, with a maximum effect at 4 hours; however, diastolic blood pressure was unaffected. The mean oral temperature had increased by a maximum of 1.2°F 4 hours after administration of the drug.

Certain features were common to the experiences of all five subjects. Subjective effects began between 1 and 2 hours after administration of the drug, with a peak between 3 and 5 hours and subsidence of effects by 7 to 8 hours. All subjects initially experienced a moderate euphoria. Perceptual effects varied but were present to some degree in all.

The subject who received 2.0 mg had the mildest reaction. He began to feel "a little high" 2 hours after taking the drug. At 3 hours he felt "a little weird; there is like a blank space between my head and body." Four hours after taking the drug, he felt normal and described his experience, "I felt good, more than usual. With my eyes closed I was pretty relaxed, and there was lots of visual imagery while listening to music. . . . It is like a half-way decent pot experience."

The three subjects who received 2.4 and 2.8 mg experienced effects similar to those described above, but the maximum effects lasted until 5 hours after the drug was taken; the effects had subsided by 8 hours. One of the subjects who received 2.4 mg first felt a change 1.5 hours after taking the drug, when he noticed that things on the wall were slightly shifting and surfaces were rippling. He described it, "Things were creeping, waving, a sort of corrugated effect. . . . I felt a little light-headed and high. . . . Sometimes the ceiling had patterns of dots which turned into real faces . . . and when I closed my eyes it was like dreaming

while awake. . . . The whole situation seems rather funny. . . . I'm cheerful, gay, exhilarated."

The subject who received 3.2 mg experienced a pronounced hallucinogenic effect like that which might occur after taking a hallucinogenic dose of lysergic acid diethylamide (LSD). Ten hours after taking the drug, he described the preceding experience, "The first effect came during lunch (2 hours after administration of the drug) when I started staring at the orange sherbet which was beautiful, brilliant orange, falling disorganizedly like a whirlpool. . . . Later (5 hours after taking the drug), I began shrinking, and water in the glass on the table was getting bigger and moving toward me, coming to envelop me. . . . I was really scared. . . . I saw a witch doctor, then a horse on the wall. . . . Then the ceiling started moving up and down and was purple and yellow. . . . I felt I was losing control." Although this subject was "coming down" at 7 hours and slept well that night after receiving glutethimide (0.5 g), he reported later that the next day he felt a mild euphoria alternating with depression. No other subject reported any lasting effects.

Regardless of the dose of DOM, about 20 percent of the ingested dose appeared in the urine within 24 hours as the unchanged compound. There was a definite peak of urinary excretion between 3 and 6 hours after administration of the drug; this peak corresponded to the peak clinical effects. If urinary excretion reflects plasma concentration, this finding suggests that DOM may be slowly absorbed into the circulation and that clinical effects are related to plasma concentrations of the unchanged drug. Aghajanian and Bing (4) have described a similar relationship between plasma concentration and mental effects of LSD.

In the Palo Alto study, 16 normal control male and female volunteers received between 2 and 14 mg of DOM as the hydrochloride in capsules with lactose filler after fasting since the previous night. The individual doses were in milligrams: 2, 3, 4, 5, 6, 8, 9, 10, 11, 12, 13, and 14. Two subjects received each of the 8, 10, and 12 mg dosages. A mood scale and psychometric measures (number facility test and flexibility of closure test) were administered before the drug was administered and 1, 3, and 5 hours after it was given. A symptom-sign questionnaire for hallu-

cinogenic effects was completed by each subject after subsidence of drug effects. At 2, 4, and 8 hours after administration of the drug, pupillary diameter, deep tendon reflexes, blood pressure, pulse rate, and oral temperature were measured. Blood specimens were collected at 2, 4, and 8 hours for determination of free fatty-acid and glucose concentrations.

In the lowest doses, DOM produced mild euphoric effects. Doses in excess of 5 mg always produced marked hallucinogenic effects whose intensity and duration were related to the dose. Effects began about 1 hour after administration of the drug, with a peak between 3 and 5 hours and subsidence by 7 to 8 hours. There were no persistent effects the next day, except in one subject who reported a mild euphoria the next morning.

Frequency and intensity of responses on the symptom-sign questionnaire summarize the clinical syndrome produced by DOM. The somatic changes included nausea, sweating, paresthesia, and tremors; perceptual changes comprised blurred vision, multiple images, vibration of objects, visual hallucinations, distorted shapes, enhancement of details, slowed passage of time, and increased contrasts. With respect to psychic effects the subjects reported that they were happy, that they lost control of thoughts at times, that they had difficulty in expressing self, that the mind was flooded with thoughts, that the mind was occasionally blank, and that they were easily distracted. Subjects seemed to have good memory for drug experience.

There was some increase in pulse rate (mean increase of 25 beats per minute) and systolic blood pressure (mean increase of 28 mm-Hg) with peak effects at 4 hours; diastolic blood pressure was unaffected. The mean increase in pupillary diameter was 15 percent at 2 and 4 hours. Although the glucose concentration in blood was unchanged, free fatty acids in the plasma doubled 4 hours after the administration of DOM.

Three subjects simultaneously received oral doses of chlorpromazine (200 mg) and DOM (10, 12, or 14 mg). All three subjects had hallucinogenic reactions which, however, appeared less pronounced than those in subjects who received the same doses without chlorpromazine. These subjects were also very drowsy. There was no accentuation of any DOM effects by chlorpromazine.

It has been rumored that chemically pure STP is more potent on a weight basis than LSD. Our studies indicate that DOM is a potent hallucinogenic agent able to produce hallucinogenic effects in doses greater than 3 mg and a mild euphoria in lower doses. This compound is chemically related to mescaline, the minimum hallucinogenic dose of which is about 300 mg in an adult. Thus, DOM is about 100 times more potent than mescaline. Since the minimum hallucinogenic dose for LSD is about 0.1 mg, DOM is only about one-thirtieth as potent as LSD.

It has been reported in the news media that effects of STP may persist for 72 hours and are intensified by chlorpromazine, which usually attenuates effects of hallucinogenic drugs. Only two of our 25 subjects reported effects persisting into the following day, and none was affected 2 days later, even though doses as high as 14 mg, more than the average amount of DOM in black-market STP pills, were administered.

It is possible that those of the "hippie" population who developed prolonged reactions to STP had been sensitized by previous experiences with hallucinogenic drugs. In the Palo Alto study chlorpromazine appeared to attenuate the effects of DOM in three subjects and definitely did not intensify them as had been reported in STP users. In our studies, chlorpromazine was administered simultaneously with DOM, while it has been given to STP users after they have already been on "bad trips." It is also possible that users of STP who developed prolonged adverse reactions accentuated by chlorpromazine had taken a drug other than DOM. Adverse reactions to atropine and related compounds may be intensified by chlorpromazine.

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