THE BLACK VAULT

161

43-Y

1-Methyl-d-lysergic acid butanolamide tartrate (UML-491, V-A-23).

Investigation of the psychotomimetic potency of this compound (methyl methergine) was undertaken because it is approximately 2.5 times as potent as LSD in blocking serotonin-induced contractions in the isolated rat's uterus and is 4.4 times as potent as LSD in blocking the serotonin-induced edema in the rat's paw (1). It was, therefore, of interest because of the hypotheses relating the LSD psychosis to serotonin blockade in the central nervous system.

METHODS

Subjects. Thirteen adult, negro male former morphine addicts without significant physical or mental disease volunteered for the experiments. All had experienced the effects of LSD in previous experiments.

B-24

Drugs. Were given in solution at 8 a.m. with the patients fasting. In preliminary experiments the dose of V-A-23 was elevated cautiously from 0.5 mg/70 kg to 5.0 mg/70 kg. In the final experiment all 13 subjects received 5.0 mg/70 kg of V-A-23.

Observations. The following observations were made at hourly intervals twice before and eight times after the drug: pupillary diameter, systolic blood pressure, threshold for the kneejerk, the LSD-questionnaire, and a short mental status examination. Methods followed were those described by Isbell et al (2), as were the methods of analyzing the data (3).

RESULTS

In the preliminary experiments no psychosomimetic effects were reported or observed with doses of 0.5 to 5.0 mg/70 kg of V-A-23 (8 subjects). In the final experiments, 2 of the 13 subjects reported psychotomimetic effects similar to those of LSD. Their symptoms included visual perceptual distortion, depersonalization, and optical hallucinations. Both were, however, very sensitive to LSD and both were regarded as being suggestible. One was a consistent placebo reactor. Significant pupillary dilatation did not occur in either instance. Symptoms in the remaining patients were not LSD-like and included sleepiness (6 of 13), nausea (4 of 13), and headache (1 of 13).

The observations are summarized in Table 1 and are compared with data obtained on 9 subjects in another experiment after placebo and 1.0 and 1.5 mcg/kg of LSD. Significant elevations in blood pressure and pupillary diameter were observed, but the change in the pupils was small, even though significant. A significant decrease in the threshold for the kneejerk also occurred.

DISCUSSION

The results are somewhat puzzling in that the pattern of change in the objective measurements was LSD-like, but was, with the exception of the 2 patients mentioned above, not correlated with mental changes of the LSD-type. It seems safe to state that if V-A-23 is a psychotomimetic, it is far less potent than LSD. Thus another example is added to the list of compounds that are potent inhibitors of peripheral actions of serotonin, but are not potent psychotomimetics.

SUMMARY

1. In doses of 71 mcg/kg (5.0 mg/70 kg), 1-Methyl-d-lysergic acid butanolamide tartrate did not consistently cause psychotomimetic effects, although significant elevations of blood pressure, decrease in the threshold for the kneejerk and dilatation of the pupils did occur.

B-23

REFERENCES

1. DOEPFNER, W. and CERLETTI, A.: Comparison of lysergic acid derivatives and antihistamines as inhibitors of the edema provoked in the rat's paw by serotonin. Internat. Arch. Allerg. and Appl. Immunol., 12: 82-97, 1958.

2. ISBELL, H., BELLEVILLE, R. E., FRASER, H. F., WIKLER, A., and LOGAN, C. R.: Studies on lysergic acid diethylamide: I. Effects in former morphine addicts and development of tolerance during chronic intoxication. A.M.A. Arch. Neurol. & Psychiat., 76: 468-478 (Nov.) 1956.

3. ISBELL, H. and LOGAN, C. R.: Studies on lysergic acid diethylamide (LSD-25). III. Attempts to attenuate the LSD-reaction in man by pretreatment with neurohumoral blocking agents. A.M.A. Arch. Neurol. & Psychiat., 81: 20-27, 1959.

Table 1.

Comparison of the Effects of 1-Methyl-d-lysergic acid butanolamide (UML-491, V-A-23) with Those of LSD-25.

MEASURE	DRUG AND DOSE (mcg/kg) Placebo[1]	LSD[1] 1.0	LSD[1] 1.5	V-A-23[2] 71.5 (5.0 mg/70 kg)
Pupillary Size	0.2 ± 1.4	10.2 ± 1.18	15.0 ± 2.1	+ 4.0 ± 1.1
Blood Pressure	+15.6 ± 13.5	64.8 ± 10.9	+94.6 ± 17.5	+ 81.9 ± 10.1
Patellar Reflex	+20.7 ± 11.1	-50.9 ± 31	-72.9 ± 21.7	- 55.8 ± 11.4
Number of Positive Responses on Questionnaire	0.1 ± 0.3	57 ± 23.2	98 ± 26.6	16.3 ± 7.6
Clinical Grade	0 ± 0	22 ± 0.38	2.8 ± 0.17	0.46 ± 0.33

1. Means ± standard errors of observations on 9 subjects.
2. Means ± standard errors of observations on 13 subjects.