

pound resembled that of a narcotic drug and none experienced a morphine-like "euphoria" at any time during substitution of No. 16298.

C. SUMMARY AND CONCLUSION

1. In doses ranging up to 400 mg. orally compound No. 16298 did not induce symptoms of morphine-like "euphoria" or behavior resembling that seen after administration of morphine in nontolerant former opiate addicts.

2. In doses of 200 and 400 mg. administered at intervals of approximately four hours, compound No. 16298 significantly suppressed the intensity of abstinence from morphine. The slight difference in the degree of depression by doses of 400 mg. as compared with doses of 200 mg. suggests that this drug would be incapable of completely suppressing symptoms of abstinence from morphine. When administered in repeated doses of 400 mg. during substitution tests definite sedative and, in some subjects, pronounced respiratory depressant effects were observed.

3. *Conclusion.*—Compound No. 16298 has addiction liability, as indicated by its ability to suppress signs of abstinence from morphine. However, its overall addiction liability is estimated to be no greater and is probably less than that of codeine.

TABLE 1.—SINGLE DOSES OF COMPOUND 16298 ORALLY

Dose (milligrams)	Number of subjects	Response
50.....	6	Negative.
100.....	2	Do.
150.....	5	Negative except 1 subject; diarrhea.
200.....	5	2 subjects slightly drowsy; 1 diarrhea.
250.....	5	1 subject slightly dizzy.
200 plus 400 ¹	2	Both complained of a light headache, but both sold, "It is like water."

¹ 200 mg were given at 8:30 a.m. and 400 mg additional were given at 9 a.m. For practical purposes the total dose was 600 mg.