follows: 260/150 to 190/110, 180/110 to 140/90, 200/115 to 180/110, 190/115 to 170/100, and 200/115 to 170/100 mm Hg.

Thus, on chronic as well as acute administration Veriloid was an active hypotensive agent, clinically similar to other Veratrum preparations previously tested.[3-5] Relative to its hypotensive effects, however, it appeared to produce somewhat less nausea and vomiting, the chief symptoms found in previous experience to interfere with the long-term usage of *Veratrum viride*. As with other preparations, meticulous adjustment of dosage to patient was the most important single point in the chronic use of Veriloid. Patients objected so strongly to the symptoms associated with overdosage that it was the practice in the present study to be satisfied with moderate lowerings of arterial pressure, rather than to attempt dramatic effects at the expense of even occasional unpleasant side reactions.

Summary. In hypertensive patients Veriloid is an active hypotensive agent when administered acutely, or chronically for periods as long as 5 months. Meticulous regulation of dosage is important in obtaining optimum results. After several weeks of continuous therapy it is frequently necessary to reduce the dosage in order to avoid nausea and vomiting. Nevertheless, relative to its hypotensive effects Veriloid seems to produce fewer toxic reactions than any other oral preparation of *Veratrum viride* presently available.

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Oral Toxicity of a New Miticide, Di-(p-chlorophenyl)methylcarbinol.* (17416)

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Di-(p-chlorophenyl)methylcarbinol(DMC) synthesized by Bergmann and Bondi,[1] and later by Grummitt *et al.*,[2] has been shown to possess marked miticidal properties.[3] A preliminary study of its acute and subacute toxicity for rats and mice, following oral administration, is the subject of this report.

Acute Toxicity. Young albino rats (80-100 g) and adult albino mice (18-22 g), of the female sex, were given single doses of DMC by stomach tube. Solutions in corn oil and suspensions in aqueous mucilage of tragacanth (2%) were used. Mice were observed for 10 days, and rats for 21 days, following intubation. The results of these experiments are shown in Table I.

With the oil solution of DMC the largest single dose tolerated by all 5 rats in a dosage group was 250 mg/kg. With the aqueous suspension one animal died following a dose of 375 mg/kg, although no fatalities resulted from dosage with 500 mg/kg. Fatalities from larger doses usually occurred 48 to 96 hours after administration. Urinary incontinence, tremors, ataxia, and impairment of righting reflexes were present for approximately 24 hours before death. Such abnormalities were not seen in animals which survived. Autopsies performed immediately after death revealed no gross pathological changes beyond

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TABLE I.
Acute Toxicity of Di-(p-chlorophenyl)methylcarbinol for Rats and Mice Following Oral Administration by Stomach Tube.

	Rats		Mice			
	Oil solution	Aq. suspension	Oil solution		Aqueous suspension	
Dose, mg/kg	Mortality ratio		Paralysis ratio	Mortality ratio	Paralysis ratio	Mortality ratio
100			0/5	0/5	0/5	0/5
175			0/5	0/5	0/5	0/5
250	0/5	0/5	0/5	0/5	2/5	0/5
375	2/5	1/5	1/5	0/5	1/5	0/5
500	2/5	0/5	1/5	0/5	2/5	0/5
750	2/5	3/5	4/5	1/5	4/5	1/5
1000	2/2	4/9	4/5	1/5	5/5	3/5

TABLE II.
Effect of a Diet Containing DMC on Weight and Ultimate Survival of Young Albino Rats.

	Avg wt in g (10 rats per group) Time in days								
% DMC in diet	0	5	10	19	26	35	42	63	70
.0	63.6	80.0	84.6	112	140	171	194	248 SE = 8.3	262 SE = 8.4
.1	63.6	73.7	85.8	113	140	176	194	226 SE = 6.5	245 SE = 7.8
.25	63.8	70.2	77.4	102(7)*	127(7)	172(4)†	177(4)	206(4)	220(4)
1.0	63.7	All dead after 72 hr							

* 3 animals dead between 10th and 19th days.
† 3 animals sacrificed 28th day.

a moderate degree of hyperemia of the peritoneum and the abdominal viscera.

Mice survived the oral administration of 500 mg of DMC per kg, both as an oil solution and as an aqueous suspension, while dosages of 750 or more mg per kg resulted in the death of one or more of the 5 animals in the dosage group. During a period of 12 to 72 hours prior to death, mild to severe motor impairment of the posterior extremities was seen. The front limbs also were involved in a few cases. The motor signs rarely developed in less than 12 hours after administration of DMC. Recovery, rather than death, followed in some cases, a situation in sharp contrast to that seen in rats.

Subacute Toxicity. Four groups of 10 young female albino rats were fed, *ad libitum,* a powdered diet† containing 1.0, 0.25, 0.1, and 0.0% of DMC, respectively. The individually-housed animals were inspected daily, and were weighed periodically, but no attempt was made to measure food consumption. The progress of these animals is recorded in Table II.

The animals receiving the highest level of DMC (1.0%) became anorexic after 24 hours. Mild depression characterized their subsequent behavior and death occurred within 72 hours. The disturbances of locomotion and equilibrium seen after large single doses of DMC were not observed here. Autopsies performed immediately after death revealed hyperemia of the abdominal viscera as the sole gross finding.

The rats given the intermediate level of DMC (0.25%) consumed noticeably less food than the controls during the first 5 days. The intake of 7 of these animals increased and grossly equalled that of the controls during the next 5 days. The remaining 3 instead

† General Mills "Checkers."

became mildly depressed and completely anorexic. They died between the tenth and nineteenth experimental days. The survivors remained normal in appearance and behavior. Three were sacrificed on the twenty-eighth day and the remaining 4 at the end of the experiment. Mild hyperemia of the peritoneum and abdominal viscera was the only gross finding at autopsy in all 10 animals. There was no gross difference in average body weight between the few survivors and the controls.

The third group of rats whose diet contained 0.1% DMC showed a slight, though not significant, weight lag on comparison with the control group at 5 days. Between this time and the ninth week the average weights of the two groups were almost equal. Statistical analysis of the difference of 22 g between the average weights at 9 weeks yielded a critical ratio‡ of 2.2 which borders on significance. One week later the weight difference was 17 g and the ratio was only 1.5. Since the experiment was terminated at this time it is impossible to say whether these differences heralded the beginning of a significant lag in weight gain, and other signs of toxicity, in the treated group. The appearance and behavior of the two groups of rats did not differ in any way. Autopsies performed when the animals were sacrificed revealed no gross evidence of pathological changes in any organs or tissues.

‡ $\frac{M_1 - M_2}{\sqrt{SE^2_{M_1} + SE^2_{M_2}}}$

Comment. These studies reveal that the toxicity of DMC is of the same order as that demonstrated by Woodard *et al.*[4] for DDT under grossly similar conditions. However, a more extensive comparison of the two compounds in the same laboratory would be necessary to determine accurately the relative toxicity of the two compounds.

Summary. 1. Rats and mice were intubated with single doses of a new miticidal compound, di-(p-chlorophenyl)methylcarbinol (DMC). The effect of graded doses on ultimate survival is discussed and the ability of large doses to produce signs suggestive of nervous impairment is described.

2. A powdered diet containing 0.1% DMC was well tolerated by growing rats during a ten week period.

3. The results compare favorably with those obtained in a similar limited study of DDT in another laboratory.

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Effects of Inunction of Alpha-Estradiol on Testes and Thyroids of Albino Rats.* (17417)

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A diverse opinion exists in regard to the effect that the administration of sex hormones has on thyroid activity. Many investigators have noted that the thyroid remains normal or shows a slight degree of hypo-activity after castration or the administration of female sex hormones.[1-10] In contrast many workers

* This work was carried out at the Department of Anatomy and Physiology, at the University of Kentucky, Lexington, under the direction of Professor R. S. Allen.

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