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Comparative Toxicity of Sixteen Specimens of *Crotalus* Venom.

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Sixteen specimens of *Crotalus* venom were obtained through the courtesy of Dr. L. M. Klauber, Curator of the Natural History Museum of Balboa Park, San Diego, California, and all of these were biologically assayed for their toxicity. One specimen contained a mixture of venoms from several species of *Crotalus;* two were taken from the *Crotalus cinereous;* and the remainder were derived from 13 different varieties of the same species. The venoms were obtained by a uniform method under identically the same conditions in each case. They were all centrifuged and then dried in a vacuum at a relatively low temperature because *Crotalus* venom, when exposed to temperatures as high as 100°F., deteriorates. Since the age of the different specimens varied, the writer had an excellent opportunity to make not only a comparative study of their toxicity but also an inquiry into the effects of the lapse of time on the keeping qualities of rattlesnake venom. The toxicity of the respective venoms for animals and plants was therefore investigated. In zoöpharmacological experiments, the writer determined the minimal lethal dose of these specimens by intraperitoneal injection in white mice and, in phytopharmacological experiments, studied the effect of solutions of *Crotalus* venom in equal parts of Shive saline and distilled water (concentrations of 1:20,000 and 1:10,000) on the growth of seedlings of *Lupinus albus* with an initial root length of from 35 to 50 mm. The phytopharmacological test has been described elsewhere.[1] In the present investigation the increment in growth of the seedling roots for 24 hours in the dark at 15°C. was taken as a criterion. Table I exhibits the data obtained regarding all the specimens of *Crotalus* venom investigated.

The dosages for mice were expressed as the average lethal dose for a mouse weighing 22 gm. It will be noted that there was a wide divergence in toxicity of the venoms for both animals and plants. The minimal lethal dose of the most toxic specimen for mice was 0.045 mg. while that of the least toxic was 0.30 mg., or nearly 6.7 times as much. This difference in toxicity obviously bears no relation to the age of the specimens, for some of those recently col-

[1] Macht and Livingston, *J. Gen. Physiol.*, 1922, **4**, 573.

TABLE I.
Comparative Toxicity of Specimens of *Crotalus* Venom.

Lot No.	Species of *Crotalus* from which Venom was Obtained	Date Collected	Minimal Lethal Dose for Mice	Phytotoxic Index of Growth of *Lupinus albus* Seedlings at 15°C. in	
				1:20,000 Venom Sol.	1:10,000 Venom Sol.
			mg.	%	%
586	Mixed *Crotalus* venoms	6- 3-35	.07	66	50
441	*Crotalus cerastes*	6-10-32	.06	87	64
540	*Crotalus mitchellii mitchellii*	8-27-33	.045	69	55
422	*Crotalus viridis viridis*	5-16-32	.045	66	59
465	*Crotalus viridis abyssus*	10-13-32	.10	59	48
489	*Crotalus cinereus*	5-21-33	.12	77	66
551	*Crotalus viridis lutosus*	10-29-33	.14	83	77
545	*Crotalus viridis oreganus*	9-10-33	.14	87	81
587	*Crotalus scutulatus*	6-10-35	.24	91	80
530	*Crotalus molossus molossus*	8-13-33	.06	87	76
518	*Crotalus mitchellii pyrrhus*	7- 9-33	.075	83	73
496	*Crotalus ruber*	7- 2-35	.11	86	79
588	*Crotalus cinereus*	6-10-35	.30	94	93
562	*Crotalus mitchellii stephensi*	4- 8-34	.12	85	78
584	*Crotalus horridus*	6- 3-35	.11	85	80
517	*Crotalus lucasensis*	7- 6-33	.12	81	80

lected were quite weak while some of the oldest were among the most potent venoms examined. Of special interest is the marked difference in toxicity of specimens 489 and 588, taken from the *Crotalus cinereus* in 1933 and 1935, respectively. The reason for this difference in toxicity of 2 specimens obtained with the same technique under parallel conditions is problematical but a number of factors, such as age, health, nutrition, light, temperature and barometric pressure, may play a rôle in this connection.[2, 3] The present research was carried on for a period of 5 months. The lethal dosage of the first 2 venoms examined, specimens 586 and 441, was discovered to be the same at the expiration of the 5-month interval as it had been at the beginning, a finding which indicated that the potency of specimens kept at a temperature of from 12 to 17°C. in the dark remained unchanged. This is not true, however, of saline solutions of *Crotalus* venom, as these rapidly deteriorate not only when exposed to sunlight but also when kept even at room temperature.

The toxicity of the different specimens for plants also varied and in general ran parallel to that which they respectively exerted on animals. However, quantitative variations were noted when their toxicity for plants and animals, respectively, was compared, differences which were to be expected since snake venoms are not single entities but are made up of several constituents, some of which may be more effective for plants as others are for animals. The study outlined above is impressive particularly in respect to the enormous variation in potency of snake venoms obtained by uniform method under the same conditions.

Summary. Sixteen specimens of dry *Crotalus* venoms from 14 different species of rattlesnake were tested biologically for their toxicity on mice and *Lupinus albus* seedlings. The different specimens varied enormously with regard to their toxicity. The dried scales of *Crotalus* venom kept in the dark and in cool containers retained their potency quite well, in some cases, even for several years.

[2] Noguchi, Snake Venoms. Carnegie Institution of Washington, 1909.

[3] Macht, *Am. J. Med. Sciences*, 1935, **189**, 520.