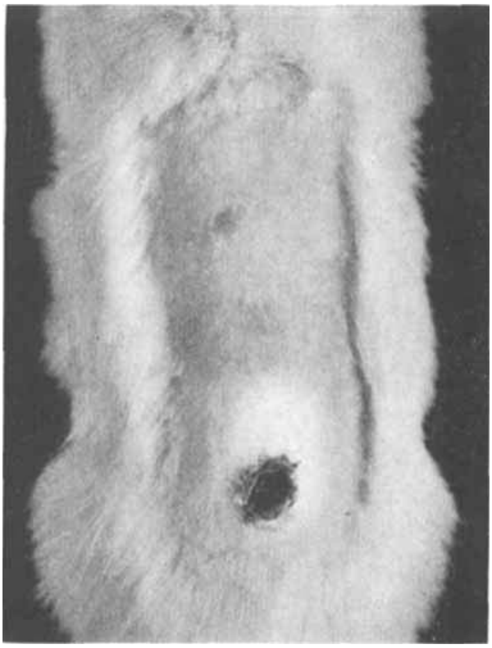

Fig. 3.—Typical Case of Definite Improvement.

aminations. These were done by Dr. George Z. Williams, associate professor of pathology, Medical College of Virginia. He examined 14 rats. Five of these died during different periods of treatment. Nine died at periods ranging from one week to twelve months after treatment. He made the following report on his examinations:

1. Animals which died during treatment: "No qualitative variations could be found to distinguish the treated and untreated irradiated rats."

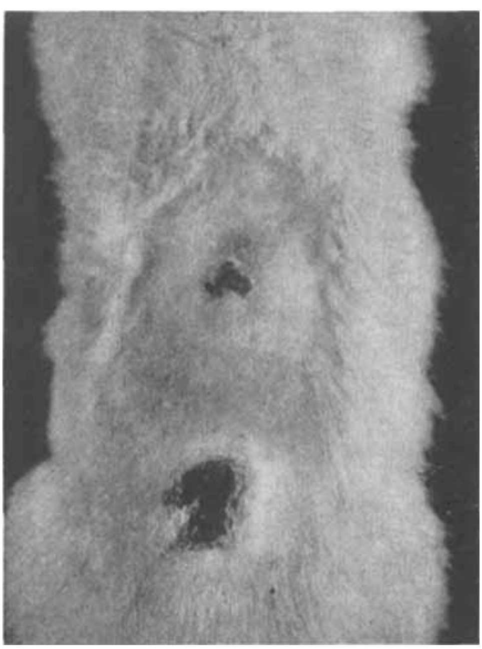

Fig. 4.—Typical Case of Slight Improvement.

2. Animals which died after treatment: "The healed scars were different histologically only in degree of fibrosis and atrophy of the skin, no qualitative changes being discernible between anterior and posterior areas."

SUMMARY

To date, no definite conclusions have been drawn from the work because: (1) too few animals have received treatment; (2) the 14-day period of treatment is too short a time on which to base final conclusions.

From the results obtained, fresh *Alœ vera* jell shows some promise of being of value in the treatment of X-ray reactions. Plans have been made to continue this problem along the lines already pursued. A larger number of animals is to be treated for a longer period of time.

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Red Squill, VII. Influence of Altitude upon Toxicity to Albino Rats*

By Justus C. Ward, H. J. Spencer, D. Glen Crabtree and F. E. Garlough

Powdered red squill (*Urginea maritima*) is used as a toxic agent for the control of rats in all parts of the country, and since it is employed as a crude powder and the

* From the Control Methods Research Laboratory, Bureau of Biological Survey, U. S. Department of the Interior.

bulbs vary considerably in their content of the rat-killing principle, frequent bioassays should be made in order to produce a reliable product. In comparing the toxicities obtained from bioassays of red squill in our laboratory in Denver, Colorado, with the results of similar tests of the same powder at a lower altitude, the percentages of kill in Denver were consistently higher than those observed at a lower elevation. On analysis of these data it became apparent that altitude is an important factor in the toxic action of red squill.

Changes in the effects of drugs due to altitude have been recognized for well over a century (1). More recently Macht reported (2), in 1931, that digitalis is more toxic to cats at high altitudes in the Blue Ridge Mountains, the Rocky Mountains and in the Tyrolean Alps than at Baltimore. Lehman and Hanzlik (3), in 1932, stated that the emetic and fatal doses of digitalis are 40% to 22% less for pigeons at an altitude of 10,000 feet than at sea level, and these authors also found the same tendencies shown by extremes of fatal doses for a limited number of cats. In 1935 Moore and Ward (4) demonstrated that strychnine is more toxic to tame albino rats and Columbian ground squirrels at an altitude of 5000 feet than at sea level. A. Cannava (5), in 1938, studied the action of chloral on adult rabbits on Mt. Etna (altitude 3000 meters) and found that its action was notably reinforced over the same dosage at sea level. In contrast to these findings, A. Rabbeno (6), in 1937, reported that the slow intravenous infusion of digilanid in guinea pigs at high altitudes resulted in an increase in the M. L. D. of 47% in ten days, the proportion gradually receding in twenty days, however, to 28.7%.

Table I.—Experiments Conducted at an Altitude of Approximately 14,200 Feet

No. and Sex	Weight, Gm.	Dose[a]	Result	No. and Sex	Weight, Gm.	Dose[a]	Result
1. M	121	250	Died	41. F	123	75	Died
2. M	134	250	Died	42. F	131	75	Died
3. M	135	250	Died	43. F	142	75	Died
4. M	143	250	Died	44. F	145	75	Died
5. M	143	250	Died	45. F	147	75	Died
6. M	146	250	Survived	46. F	150	75	Died
7. M	147	250	Survived	47. F	150	75	Died
8. M	153	250	Died	48. F	152	75	Died
9. M	158	250	Died	49. F	152	75	Died
10. M	162	250	Survived	50. F	155	75	Died
11. M	145	200	Died	51. F	112	50	Died
12. M	147	200	Died	52. F	125	50	Survived
13. M	150	200	Survived	53. F	132	50	Died
14. M	152	200	Died	54. F	135	50	Died
15. M	152	200	Survived	55. F	146	50	Died
16. M	153	200	Died	56. F	150	50	Died
17. M	155	200	Died	57. F	155	50	Survived
18. M	163	200	Died	58. F	157	50	Died
19. M	165	200	Died	59. F	164	50	Died
20. M	170	200	Died	60. F	177	50	Died
21. M	128	150	Died	61. F	104	40	Died
22. M	138	150	Died	62. F	126	40	Survived
23. M	140	150	Died	63. F	131	40	Survived
24. M	141	150	Died	64. F	135	40	Died
25. M	141	150	Survived	65. F	144	40	Survived
26. M	144	150	Died	66. F	146	40	Survived
27. M	145	150	Died	67. F	152	40	Died
28. M	148	150	Died	68. F	156	40	Died
29. M	150	150	Died	69 F	160	40	Died
30. M	157	150	Died	70. F	164	40	Died [b]
31. M	165	100	Survived	71. F	113	25	Survived
32. M	168	100	Died	72. F	114	25	Survived
33. M	170	100	Died	73. F	115	25	Survived
34. M	173	100	Died	74. F	115	25	Survived
35. M	177	100	Survived	75. F	122	25	Survived
36. M	183	100	Died	76. F	125	25	Survived
37. M	185	100	Survived	77. F	126	25	Survived
38. M	200	100	Survived	77. F	133	25	Died
39. M	213	100	Survived	79. F	142	25	Survived
40. M	215	100	Survived	80. F	164	25	Survived

[a] Milligrams of red squill powder per kilogram of body weight.
[b] More than 80% of the animals listed above this line died, while less than 50% of those listed below this line succumbed.

Table II.—Experiments Conducted at an Altitude of 717 Feet

No. and Sex		Weight, Gm.	Dose[a]	Result	No. and Sex		Weight, Gm.	Dose[a]	Result
81.	M	206	1250	Died	131.	F	132	800	Died
82.	M	210	1000	Died	132.	F	166	700	Died
83.	M	223	750	Died	133.	F	145	600	Died
84.	M	214	750	Died	134.	F	165	500	Died
85.	M	229	717	Died	135.	F	167	500	Died
86.	M	230	695	Died	136.	F	155	400	Died
87.	M	219	610	Died	137.	F	153	400	Died
88.	M	238	500	Died	138.	F	158	300	Died
89.	M	221	500	Died	139.	F	172	200	Died
90.	M	233	250	Survived	140.	F	160	100	Died
91.	M	169	700	Died	141.	F	131	100	Survived
92.	M	173	700	Died	142.	F	140	100	Survived
93.	M	182	700	Died	143.	F	146	100	Died
94.	M	189	700	Died	144.	F	158	100	Died
95.	M	204	700	Died	145.	F	161	100	Died
96.	M	205	700	Died	146.	F	165	100	Died
97.	M	213	700	Died	147.	F	165	100	Died
98.	M	214	700	Died	148.	F	172	100	Died
99.	M	226	700	Died	149.	F	173	100	Died
100.	M	228	700	Died	150.	F	176	100	Died
101.	M	134	600	Died	151.	F	110	50	Died
102.	M	182	600	Survived	152.	F	146	50	Died
103.	M	183	600	Died	153.	F	152	50	Survived
104.	M	187	600	Died	154.	F	153	50	Survived
105.	M	192	600	Died	155.	F	163	50	Died
106.	M	193	600	Died	156.	F	164	50	Died
107.	M	207	600	Died	157.	F	165	50	Died
108.	M	219	600	Died	158.	F	167	50	Survived
109.	M	220	600	Survived	159.	F	171	50	Survived
110.	M	224	600	Died	160.	F	172	50	Died
111.	M	162	400	Died					
112.	M	177	400	Survived					
113.	M	177	400	Survived					
114.	M	188	400	Died					
115.	M	190	400	Died					
116.	M	195	400	Survived					
117.	M	210	400	Survived					
118.	M	215	400	Died					
119.	M	221	400	Survived					
120.	M	248	400	Survived					
———[b]									
121.	M	159	250	Survived	161.	F	126	25	Survived
122.	M	162	250	Survived	162.	F	170	25	Survived
123.	M	177	250	Survived	163.	F	170	25	Survived
124.	M	179	250	Survived	164.	F	172	25	Survived
125.	M	203	250	Survived	165.	F	183	25	Survived
126.	M	205	250	Survived	166.	F	186	25	Survived
127.	M	207	250	Survived	167.	F	187	25	Survived
128.	M	213	250	Survived	168.	F	193	25	Survived
129.	M	216	250	Survived	169.	F	194	25	Survived
130.	M	216	250	Survived	170.	F	201	25	Survived

[a] Milligrams of red squill powder per kilogram of body weight.
[b] More than 80% of the animals listed above this line died, while less than 50% of those listed below this line succumbed.

Table III.—Comparison of Results

Location and Altitude, Feet	Males				Females			
	Dosage[a] Range	Percentage of Kill	Dosage[a] Range	Percentage of Kill	Dosage[a] Range	Percentage of Kill	Dosage[a] Range	Percentage of Kill
Mt. Evans, Colo., 14,200	150–200	80	100	40	40–75	80	25	10
Denver, Colo., 5280	250	87	200	47	75	87	50	47
Winchester, Va.,	600–700	90	250–400	20	100	80	25–50	30

[a] Milligrams of red squill powder per kilogram of body weight.

In order to study the influence of altitude on the toxic action of red squill, toxicity determinations were carried out at the Cosmic Ray Laboratory of the University of Denver, located on top of Mt. Evans, Colorado, at an elevation of approximately 14,200 feet; at Denver, Colorado, elevation 5280 feet; and at Winchester, Virginia, altitude 717 feet.

EXPERIMENTAL

Rats used in these experiments were from Denver stock and were kept upon the same diet of fox chow throughout this entire study. The rats from the Denver colony were taken to the Mt. Evans laboratory and allowed to remain at that altitude six days before being used for toxicity determinations. Rats, with an adequate supply of food, were shipped from Denver to Winchester, Virginia, and were allowed thirty days for acclimatization before being used for toxicity studies. The red squill used in these determinations was a standardized powder prepared in the Denver laboratory from a single bulb of high potency. The experiments were carried out using the same technique as reported in a previous paper (7). Data obtained at Mt. Evans and at Winchester, Virginia, were compared with those obtained in the Denver laboratory on the same red squill preparation. The results of the Denver experiments were previously reported in the study of sex factors in the toxicity of red squill (7).

DISCUSSION

The quantities of red squill fed were chosen in such a manner that 75% of the doses given were in the range in which from 80% to 90% of the animals were killed and 25% in the range in which most of the animals survived. These ranges were determined by preliminary experiments in which graduated doses were used. The latter series, one for each sex, are reported in Table II (males, numbers 81–90; females, 131–140, inclusive). In all cases the animals were fasted twenty-four hours before the experiments. The comparison of results given in Table III clearly shows that white rats taken from the same Denver colony to the top of Mt. Evans (altitude 14,200 feet) and to Winchester, Virginia (altitude 717 feet) varied decidedly in their resistance to red squill powder. The findings at Denver, Colorado (altitude 5280 feet), were intermediate between those obtained at the extremes of altitude, as is demonstrated by the fact that 80–90% of the male rats were killed at a dosage of 150–200 mg./Kg. on Mt. Evans, at 250 mg./Kg. in Denver and at 600–700 mg./Kg. in Winchester. Also, in the lower concentrations at which the red squill powder was used, 40% of the male rats were killed at 100 mg./Kg. on Mt. Evans, 47% at 200 mg./Kg. in Denver and only 20% at 250–400 mg./Kg in Winchester. These results indicate that male rats are approximately three times as resistant to red squill at an altitude of 717 feet as they are at 14,200 feet, and about twice as resistant at 717 feet as at 5280 feet. The experiments on female rats at the three elevations demonstrated tendencies in the same direction, but the differences were much less marked.

CONCLUSIONS

1. Altitude is an important factor in the toxicity of powdered red squill to white rats.
2. The influence of altitude is shown primarily on the toxicity to the male rats.
3. The susceptibility of females is little changed by wide variations in altitude.
4. Considerable differences in altitude must be considered in the interpretation of bioassays of red squill powder.

ACKNOWLEDGMENTS

The high altitude studies were made possible through permission given us by Dr. Joyce C. Stearns, in charge of the Cosmic Ray Laboratory of the University of Denver, located 65 miles west of Denver, Colorado, on the top of Mt. Evans, to use the facilities of this laboratory.

We also appreciate the six-day animal care given our experimental rats by Arnold Mathees and Sherman Sundet, Cosmic Ray Laboratory attendants.

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