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Lack of Effect of Sodium Phenosulfazole (Darvisul) on Certain Experimental Virus Infections.*

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Sodium phenosulfazole, or Darvisul, (N-(2-thiazolyl)-phenol sulfonamide)† has recently been described by Sanders, SubbaRow and Alexander[1] as protecting mice against as many as 100 LD_{50} doses of the Columbia SK murine virus.

The present report is concerned with tests of Darvisul against the MM virus,‡ the Lansing strain of poliomyelitis virus, and Theiler's virus of mouse encephalomyelitis (TO strain). No protective effect was found.

CFW mice (Carworth Farms) 5 to 6 weeks old, weighing 15 to 20 g were used in all but one experiment. Eight mg of Darvisul in 1 ml of physiologic saline were given twice daily by the intra-abdominal route. In the experiment on Theiler's virus (Table II) 3 to 4 week old mice were used conforming to our standard procedure with TO virus and the drug was fed in the diet.

In Experiment 1 (Table I) the procedure described by Sanders and his associates[1] was followed precisely, *e.g.* 8 mg of Davisul were given twice daily beginning 24 hours after intra-abdominal injection of MM virus and continued for 5 days. No significant difference was observed in the treated and control animals. In Experiments 2 and 3, Darvisul was begun 2 days before and continued for 6 days after infection. The suggestive difference obtained in Experiment 2 was not reproduced in Experiment 3. In Experiments 4 and 5, MM virus was given by a route different from that of Darvisul—subcutaneously and by mouth, respectively. No appreciable effect was noted. The *in vitro* effect of Darvisul on MM virus was tested in Experiment 6. Instead of inactivation of virus, the titer of the suspension of virus plus Darvisul was more than 100 times greater than the titer of the virus control. In Experiment 7, Darvisul was begun 2 days before and continued for 6 days after intracerebral injection of the Lansing strain of poliomyelitis virus. The results were negative. Experiment 8 is concerned with Theiler's virus of mouse encephalomyelitis as found in the intestines of normal mice (Table II). The capacity of Darvisul to reduce the amount of TO virus excreted in the feces was tested. The stools of individual mice were assayed for virus before and after drug administration. In this experiment a 2% drug diet was fed to 3 mice for 7 days. The amount of Darvisul consumed was 72 to 88 mg per day. In contrast to certain other compounds tested in this laboratory,[4] Darvisul had no effect upon the excretion of TO virus in the feces of these mice.

Summary. Under the circumstances which have been described, Darvisul revealed neither prophylactic nor therapeutic value in mice infected with the MM virus, the Lansing strain of poliomyelitis virus or Theiler's virus of mouse encephalomyelitis (TO).

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1 Sanders, M., SubbaRow, Y., and Alexander, R. C., *Texas Reports on Biology and Medicine*, 1948, **6**, 385.

‡ MM virus has been shown to be closely related serologically to Columbia SK virus and the virus of encephalomyo-carditis.[2,3]

2 Warren, J., and Smadel, J. E., *Fed. Proc.*, 1948, **7**, 311.

3 Ward, R., and Rader, D. L., unpublished work.

4 LoGrippo, G. A., Earle, D. P., Jr., Brodie, B. B., Graef, I. P., Bowman, R. L., and Ward, R., unpublished work.

TABLE I.
Lack of Effect of Darvisul on MM Virus and Lansing Poliomyelitis Virus Infection in Mice.

Exp. No.		Darvisul: Dose, mg/day	Darvisul: Drug route	Infection: Virus route	Infection: Virus Strain	Conc. of virus: 10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}	LD_{50} titer	Remarks
1	Control	0	—	IP	MM			15/15*	15/15	14/14	11/12		$10^{-6.5}$ or more	Drug admin. begun 24 hr after infection and continued 5 days.
	Treated	16	IP	,,	,,			15/15	14/15	13/13	9/14		$10^{-6.2}$ or more	
2	Control	0	—	,,	,,				10/10	9/10	4/10		$10^{-5.7}$	Drug admin. 2 days pre and 6 days post infection.
	Treated	16	IP	,,	,,				7/9	2/10	1/9		$10^{-4.6}$	
3	Control	0	—	,,	,,				10/10	7/10	2/10	1/10	$10^{-5.5}$	Ditto No. 2.
	Treated	16	IP	,,	,,			10/10	10/10	7/10	5/10	1/10	$10^{-5.8}$	
4	Control	0	—	SC	,,					9/9	8/10	4/10	$10^{-6.7}$	Ditto No. 2.
	Treated	16	IP	,,	,,					9/9	7/10	2/9	$10^{-6.4}$	
5	Control	0	—	oral	,,		4/9	1/8						Ditto No. 2.
	Treated	16	IP	,,	,,		6/10	6/10						
6	Control	*In vitro* exper.		IP	,,		6/6	6/6	4/6	0/6	0/6		$10^{-4.2}$	1% virus vs. 1% drug at 37°C for 2 hr after which dilutions were made with distilled water.
	Treated			,,	,,		6/6	6/6	6/6	6/6	5/6		$10^{-6.4}$ or more	
7	Control	0	—	IC	LA	7/8	4/8	0/8	0/8				$10^{-1.7}$	Ditto No. 2.
	Treated	16	IP	,,	,,	7/7	2/8	0/8	0/8				$10^{-1.7}$	

* 15/15 Numerator = number of mice paralyzed; denominator = number of mice inoculated. Mice dying without symptoms have been excluded.
IP = Intraperitoneal; IC = Intracerebral; SC = Subcutaneous; LA = Lansing poliomyelitis virus.

TABLE II.
Lack of Effect of Darvisul on the Excretion of Theiler's Virus (TO).

Exp. No.	Darvisul: Individual mice treated	Darvisul: Average dose drug/day, mg	Assay of TO virus in feces of individual mice: Before Darvisul	Assay of TO virus in feces of individual mice: After 7 days of Darvisul
8	Mouse No. 1	88	8/10*	8/10
	,, ,, 2	74	2/9	1/7
	,, ,, 3	72	10/10	9/9

* 8/10 = 8 out of 10 mice became paralyzed following inoculation of feces from mouse No. 1.