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Alcoholate of Trimer of Hydroxypyruvic Aldehyde as Antidote in Mercuric Chloride Poisoning.

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A method for the purification of the alcoholate of the trimer of hydroxypyruvic aldehyde[1] and a study of the metabolism of this compound[2] have been reported.

The compound depolymerizes readily in aqueous solution, yielding 2 mols of hydroxypyruvic aldehyde and 1 mol of the alcoholate of the monomer and will therefore be referred to as hydroxypyruvic aldehyde. The aqueous solution reduces mercuric chloride rapidly in the cold, especially in the presence of disodium phosphate.

This investigation was undertaken to determine the capacity of hydroxypyruvic aldehyde and disodium phosphate to act as an antidote in experimental mercuric chloride poisoning.

Experimental. The experiments were performed on rabbits and cats. All animals were fasted during the 18 hours prior to experimental use, excepting 2 rabbits which were fasted for 48 hours. Mercuric chloride was administered by stomach tube in all of the experiments. Hydroxypyruvic aldehyde and disodium phosphate were given consecutively, whether administered orally or intravenously. Oral doses were followed by a wash of 1 cc of water.

1. *Rabbit Experiments.* In this series of experiments mercuric chloride was administered in 1% solution, hydroxypyruvic aldehyde in 5% solution and disodium phosphate in 5% solution.

Blood urea-nitrogen levels were determined by Karr's direct Nesslerization method.[3] These are recorded in Table II.

The respective groups of rabbits were treated with the antidote orally and intravenously 15, 30, and 60 minutes after the administration of mercuric chloride. These dosages are recorded in Table I. In most cases oral treatment with the antidote was repeated.

2. *Cat Experiments.* In this series of experiments each cat received 5 mg of morphine sulfate per kg of body weight subcutaneously

[1] Evans, W. E., Jr., Carr, C. J., and Krantz, J. C., Jr., *J. A. C. S.*, 1938, **60**, 1628.

[2] Evans, W. E., Carr, C. J., and Krantz, J. C., Jr., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 573.

[3] Karr, W. G., *J. Lab. Clin. Med.*, 1924, **9**, 3.

TABLE I.
Dosages of Substances Administered to Rabbits.

Substance	Dosage (mg/kg)	
	Oral	Intravenous
Mercuric Chloride	20	0
Hydroxypyruvic Aldehyde	500	125
Disodium Phosphate	250	65

one hour before the experimental poisoning in order to prevent vomiting. Mercuric chloride was administered in 2% solution and hydroxypyruvic aldehyde and disodium phosphate in 10% solution.

Groups of cats were treated with hydroxypyruvic aldehyde and disodium phosphate at intervals of 1, 5 and 15 minutes respectively, after the administration of a fatal dose of mercuric chloride. The results are shown in Table III.

Discussion. Autopsies performed on rabbits No. 10, No. 21, and No. 24 showed no gross pathology of the gastrointestinal tract or kidneys. On examination of rabbit No. 10 the liver was found to be highly parasitized and there were hemorrhagic patches on the lungs. Death of rabbits No. 23 and 25 on the eleventh day of the experiments may have been caused by unusually hot weather. This conclusion is supported by the blood-urea-nitrogen determinations made on the ninth day. These determinations indicated that there was slight or no renal impairment at this time.

Treatment of 11 rabbits with hydroxypyruvic aldehyde and disodium phosphate one hour after the administration of mercuric chloride prevented renal injury in 9 animals. Decreased chance of survival after prolonged fasting is indicated by the blood urea-nitrogen levels of the 2 animals which had been fasted for 48 hours prior to experimental poisoning. Oral treatment with the antidote again on the second day of the experiment may favor recovery.

Oral treatment of 11 cats with hydroxypyruvic aldehyde and disodium phosphate one minute after the administration of mercuric chloride prevented acute poisoning. Nine animals survived longer than 30 days. The other 2 cats died on the seventeenth and twenty-fourth days, respectively, of the experiment. The antidote did not protect cats effectively if 5 minutes had elapsed before treatment but did increase the average survival time. Hydroxypyruvic aldehyde and disodium phosphate had no antidotal action when administered 15 minutes after mercuric chloride had been given.

Conclusions. Hydroxypyruvic aldehyde in the presence of disodium phosphate acted, within the limits set forth in these experiments, as an effective antidote against mercuric chloride poisoning in rabbits and cats.

TABLE II.

Blood Urea-Nitrogen Determined on Rabbits Poisoned with Mercuric Chloride and Subsequently Treated with Hydroxypyruvic Aldehyde and Disodium Phosphate.

No. rabbits in group	Time bet. adm. of poison and antidote, min.	Rabbit No.	Survival period, days	Blood urea-nitrogen (mg%)								Remarks
					Day of experiment							
				Control	2	3	4	5	6	7	9	
3		6	3	16.8	—	218	534					
		7	2	23.2								
		8	3	15.9	—	276						
3	15	12	1	17.4								Only phosphate adm.
		13	>30	7.6	—	14.3	17.6	—	21.0			Oral antidote repeated 2nd and 3rd days
		14	4	5.2	—	172	237					
3	15	9	>30	21.8	—	19.0	14.8	—	18.5			
		10	4	6.0	—	32.1	24.2					Oral antidote repeated 2nd and 3rd days
		11	>30	7.7	—	18.6	12.3	—	14.6			
3	30	15	>30	19.2	35.9	12.3	—	15.3				
		16	14	22.6	37.5	57.0	—	61.6				Oral antidote repeated 2nd day
		17	>30	18.8	33.2	16.3	—	10.4				
		18	5	24.1	53.0	—	>100	—	279			
		19	>30	20.3	26.2	—	15.6	—	—	14.2		Oral antidote repeated 2nd day
		20	>30	13.2	20.4	—	13.9	—	—	12.4		
		21	>20*	11.4	20.6		13.6	—	—	12.0		
		22	>30	18.9	20.2		14.8	—	—	19.4		
11	60	23	11	19.7	35.2	23.5	—	—	—	—	24.8	
		24	12*	16.7	38.0	47.5	—	27.3	—	—	30.6	
		25	11	11.3	22.2	—	—	15.9	—	—	14.4	
		26	1	14.6								
		33	>30	19.2	—	—	123	—	73.0	—	66.6	Fasted 48 hrs
		34	>30	17.2	—	—	82	—	47.5	—	52.8	Oral antidote repeated after 5 hrs

> More than.

* Sacrificed for autopsy.

TABLE III.
Antidote After Oral Administration of Mercuric Chloride to Cats.

Cats in group No.	Dose of mercuric chloride, mg/kg	Time interval bet. adm. of poison and antidote, min	Antidote (mg per kg)				Survival period		Avg survival period in fatal cases, days
			Hydroxypyruvic aldehyde		Disodium phosphate		Cats No.	Days	
			Oral	I.V.	Oral	I.V.			
3	25		0	0	0	0	1	1	1.7
							2	2	
3	0		250	62	125	31	3	>30	
6	25	5	250	62	125	31	2	1	8.5
							1	3	
							1	4	
							1	14	
							1	28	
5	25	15	250	62	125	31	1	1	2.0
							3	2	
							1	3	
12	25	15	500	0	250	0	5	1	2.3
							4	4	
							3	>30	
4	25	5	500	0	250	0	2	2	7.0
							1	10	
							1	14	
11	25	1	500	0	250	0	1	17	20.5
							1	24	
							9	>30	

Each cat received 5 mg of morphine sulfate per kg body weight subcutaneously one hour before mercuric chloride was administered.